

# EMJ Radiology

## Editor's Pick

Imaging of Ovarian Cancer:  
From Early Detection to  
Post-treatment Relapse

## Interviews

Interventional radiologist  
Fred T. Lee Jr shares  
insights from his career  
and his perspective on  
the field of radiology

Review of  
ECR Congress 2022



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EMJ is published quarterly and comprises review articles, case reports, practice guides, theoretical discussions, and original research.

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Editor

We are pleased to share with you our 2022 issue of *EMJ Radiology*. This issue highlights research findings in radiology across clinical disciplines, from reproductive health and urology to oncology and neurology. We also share our review of the European Congress of Radiology (ECR) 2022 to spotlight some of the key discussions from the event.

ECR 2022 was split into two events this year, with a prelude to the main congress held in March this year before the main event in July in Vienna, Austria. Covering both events for EMJ showcased the rich array of research fields in radiology, and the theme of ECR 2022, 'building bridges', tied into the multidisciplinary work of radiology across clinical fields. In this issue we provide selected abstracts from ECR 2022, summarised by the authors themselves, alongside our featured summary of a key session from the congress: The Role of Radiologists in Screening Programmes for Lung and Prostate Cancer.

This issue also shares our interview with Fred T. Lee Jr., University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA, who discusses his work as a founding member of the International Working Group for Tumour Ablation and his experience in interventional radiology.

Our Editor's Pick article for this issue is a review by Rosemarie Forstner, 'Imaging of Ovarian Cancer: From Early Detection to Post-treatment Relapse,' which provides a practical analysis of the role for imaging throughout the disease course. Other research articles included consider topics of percutaneous nephrostomy insertion training and epidemiology-led paediatric brain MRI reporting.

As always, I would like to express my thanks to our authors who have contributed to this issue and to our Editorial Board and peer reviewers for their work in ensuring the high quality of the journal. I hope you enjoy this latest issue of *EMJ Radiology*. We look forward to seeing you at next year's ECR in Vienna.

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# Foreword

Dear Colleagues,

Welcome to the latest issue of *EMJ Radiology*. Here, we feature content from the European Congress of Radiology (ECR) Congress 2022, which returned this year both virtually and onsite in the wonderful city of Vienna, Austria.

This issue brings with it excellent content from radiology colleagues all over the world. An invaluable paper by Biyani et al. discusses different approaches to percutaneous nephrostomy insertion, the challenges that can be faced by trainees, and the merits of *ex vivo* models of training, which promote a safe and risk-free environment in which to learn. Dilip et al. present the case study of a 44-year-old female with a rare primary malignancy cholangiocarcinoma, and discuss what they believe to be the first instance of facial metastasis in this disease.

Maheshwari et al.'s epidemiological study discusses the difficulty of capturing reliable brain MRIs in the child population, examining the ways in which contextual reporting of neuroimaging in paediatric patients may improve both accuracy and speed. Forstner examines ovarian cancer imaging, from possible early

detection to relapse following treatment. Ovarian cancer tends to be diagnosed at a later stage when the prognosis is poor. Imaging provides a wealth of information throughout the disease cycle in regard to treatment planning, the possibility of relapse, and the eligibility of patients for cytoreductive surgery.

Cassar-Pullicino et al. present a retrospective study examining loose bodies resulting from osteochondral injury, which can migrate to adjacent compartments in the body. This case series pinpoints over 30 cases where loose bodies migrated within the flexor hallucis longus tendon sheath, and were identified using a CT scan, MRI, or ultrasound.

As well as a fascinating interview with Fred T. Lee Jr., University of Wisconsin, USA, we present a wealth of coverage from ECR 2022, including late-breaking abstracts, insightful features, and novel interviews from key players in ECR.

I extend my gratitude to all of those who have contributed to this fascinating issue of *EMJ Radiology*, and sincerely hope that you enjoy reading the journal.



**Yasmeen Malik**

St. Georges University of London, UK



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# EMJ



# ECR 2022



## Review of the European Congress of Radiology (ECR) 2022

**Location:** Vienna, Austria

**Date:** 13<sup>th</sup>–17<sup>th</sup> July 2022

**Citation:** EMJ Radiol. 2022;3[1]:9-17. DOI/10.33590/emjradiol/10185412.  
<https://doi.org/10.33590/emjradiol/10185412>.

'BUILDING bridges' was the running theme of the European Congress of Radiology (ECR) 2022. This theme was carried throughout a special range of sessions that focused on the interaction between radiologists and other specialists, but also within radiology, improving practice, patient outcomes, and efficiencies. Building bridges is a fundamental aspect of working towards the future, allowing radiologists to take on a more important role than ever before with clinical workers, policymakers, patients, and industry.

The opening ceremony began with a welcome from the European Society of Radiology (ESR) President, Regina G.H. Beets-Tan, who spoke to attendees located in the audience in Vienna, Austria, but also those attending virtually from around the globe. She emphasised the importance of fortitude, collaboration, and unity from the medical professionals in the wake of ongoing events in Europe, underlining the value and opportunity that congresses such as the ECR provide for this collaboration. Reflecting on the history of radiology as a therapy area, Beets-Tan discussed the growth of the specialty over the last 30 years, filling in the gaps between cutting edge advanced imaging and clinical practice at the time.

New digital technologies, such as artificial intelligence (AI), were emphasised for their ability to shift focus from value-based radiology, perfecting performance and providing opportunities for rapid data sharing across the world. The ECR 2022 featured over 1,000 experts from both within and without the radiology specialty, contributing to the overarching theme of multidisciplinary collaboration and bridge building. Education sessions featuring specialists from over 100 disciplines provided the largest opportunity for peer learning and knowledge sharing. ECR 2022 focused on interactivity, with open forums featuring young radiologists, radiographers, and ESR leaders; and roundtable discussions on pressing issues with leaders and policy makers from the European Union (EU). Patient

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**"The ECR 2022 featured over 1,000 experts from both within and without the radiology specialty contributing to the overarching theme of multidisciplinary collaboration."**

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engagement and patient consideration were highlighted with the 'Patients in Focus' programme, and new technology was exhibited in the AI theatre. Beets-Tan further underlined the value of diversity in the congress community, both geographically and professionally. Encouraging different viewpoints, innovation, and building bridges towards the future allows the ESR to advance together with industry partners, international societies, and political networks.

The opening ceremony featured an awards ceremony where extraordinary individuals were praised for their contributions to the field with ESR Honorary Memberships. Firstly, Mary C. Mahoney, Professor of Radiology, University of Cincinnati College of Medicine, Ohio, USA, who has dedicated much of her career to moving breast imaging forward and who contributed to the ECR educational programme, was given an honorary ESR membership. Secondly, Xiao-Yuan Feng, Chairman of the Department of Radiology, Huashan Hospital, Fudan University, Shanghai, China, was recognised for his contributions to global radiological societies and editing positions at radiological journals. Finally, Manuel De Souza Rocha, Associate Professor of Radiology, Universidade de São Paulo, Brazil, was praised for his advocacy of multidisciplinary practice and the exchange of skills, particularly focusing on bowel cancer.

The highest awards given by the ESR, the ESR Gold Medals, were awarded to Laura Oleaga, Head of Imaging CoreLab, Barcelona Clinical Coordinating Centre, MonClinic Foundation, Spain; Bernd Hamm, Head of CharitéCentrum 6, Universitätsmedizin Berlin, Germany; and Luis Martí-Bonmatí, Director of the Medical Imaging Department and Director of Radiology, La Fe University and Polytechnic Hospital, Valencia, Spain. Oleaga's work in pre- and postgraduate education, commitment to multidisciplinary practice, and position

on the ESR education committee working to standardise training for radiology professionals has earned her huge respect within her field, with Beets-Tan describing her as the perfect example of how radiology practice should look in the future. Hamm was praised for his work translating research into clinical practice whilst always considering patient care, and Martí-Bonmatí was commended for his work in technology, the growth of AI, and his leadership in radiological societies.

Beets-Tan closed the opening ceremony by reminding the guests to take advantage of the wide variety of opportunities available to explore over the next 4 days of the congress. She underlined that attendees should "build bridges with colleagues and friends, build bridges with clinical partners and patients, build bridges with societies and international organisations, build bridges with industry partners." This, she stated, would allow the collective ESR community to move closer to the future of radiology. ●

**"Encouraging different viewpoints, innovation, and building bridges towards the future allows the ESR to advance together with industry partners, international societies, and political networks."**



# Multi-Colour Magnetic Particle Imaging for Detection of Gastrointestinal Haemorrhage

FASCINATING research on imaging techniques for gastrointestinal (GI) haemorrhage was presented at ECR 2022. Taking place from 13<sup>th</sup>–17<sup>th</sup> July, researchers from the University Medical Center Hamburg-Eppendorf, Hamburg, Germany, shared insights into their findings of multi-colour magnetic particle imaging (MPI) for real-time detection of the condition.

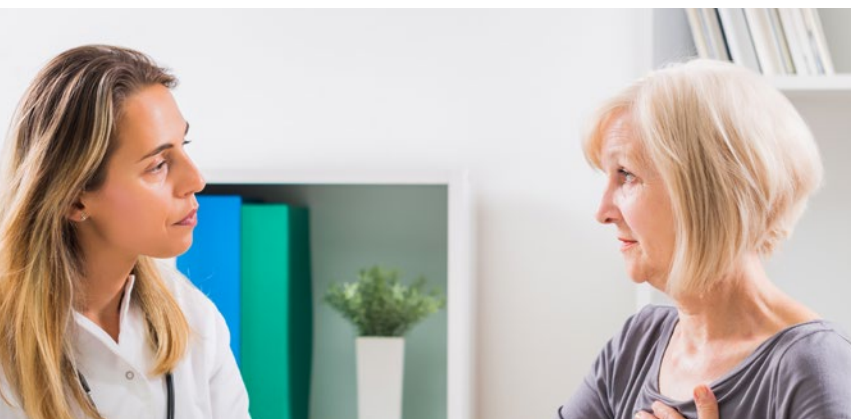
The occurrence of GI haemorrhage can be life-threatening to patients and requires rapid diagnosis and evaluation. Current methods for diagnosis include invasive endoscopic techniques, which may not enable imaging of the full GI tract, and CT angiography as a method using ionising radiation. As well as being a radiation-free technique, MPI imaging offers the advantage of multi-contrast cross-sectional imaging using superparamagnetic tracers at a high spatiotemporal resolution, enabling radiologists to detect multiple tracers.

Led by Christoph Reidel, Department of Diagnostic and Interventional Radiology and Nuclear Medicine, University Medical Center Hamburg-Eppendorf, the researchers' hypothesis focused on the use of single- and multi-contrast MPI to enable 3D real-time detection for GI bleeding. An *ex vivo* study was performed using a bowel phantom consisting of a luminal compartment and a vascular compartment to mimic the lumen and perfused bowel wall,

in which blood pool tracers were injected. The researchers also used a ligated porcine small bowel specimen with cannulated mesentery vessels to facilitate intravascular and intraluminal tracer injection. Dynamic imaging was performed using a preclinical MPI.

The results presented showed a clear enhancement of the bowel wall, with no tracer extravasation into the control lumen. In the case of GI bleeding, an extravasation of the blood pool tracer into the lumen was observed, with multi-contrast MPI showing the mixing of tracers and indicating the presence of a GI haemorrhage. Graphical evidence presented by Reidel showed the normalised signal intensity in the bowel and lumen. The GI bleed showed the tracer signal intensity increase in the phantom bowel wall, with the multi-tracer signals intersecting within the phantom lumen. The small bowel specimen showed similar results, with tracer signal intensity mixing with the presence of a GI bleed.

Reidel presented the study conclusions, which indicated that single- and multi-contrast MPI is a feasible technique to visualise real-time 3D bowel wall perfusion, both in the phantom bowel and specimen. He also noted that this may emerge as a radiation-free tool for non-invasive detection of acute and chronic GI haemorrhage. ●




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**"The results presented showed a clear enhancement of the bowel wall, with no tracer extravasation into the control lumen."**

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## PTEN Hamartoma Tumour Syndrome: The Role of MRI

*PTEN* hamartoma tumour syndrome (PHTS) is rare, with one in 200,000 individuals worldwide having pathological *PTEN* variants. Having a pathological variant of *PTEN* poses a lifetime breast cancer risk of 85% and has also been associated with higher rates of benign breast disease.

Retrospective study data presented by Alma Hoxhaj, Department of Medical Imaging, Radboud University Medical Center, Nijmegen, the Netherlands, and Department of Radiology, Netherlands Cancer Institute, Amsterdam the Netherlands, at ECR 2022, Vienna, Austria, on 16<sup>th</sup> July highlighted how MRI features in females with PHTS could assist with early breast cancer diagnosis and reduce the number of biopsies these patients undergo.

The team investigated imaging features of benign and malignant breast lesions in patients with PHTS. They recruited females aged 18 years and over with either a confirmed *PTEN* pathogenic variant or clear clinical PHTS phenotype, who had been referred to a specific Radboud University Medical Center clinic between 2001 and 2021.

A total of 65 females were included in the study and the corresponding available MRI images were read independently by two radiologists. Of these 65 individuals, 21 patients (32%) had a previous diagnosis of histology-confirmed breast cancer and 23 patients (35%) had histology-confirmed diagnosis of benign breast disease.

### "MRI features in females with PHTS could assist with early breast cancer diagnosis and reduce the number of biopsies these patients undergo."

Thirty-five breast cancers were identified from the 21 females with previous breast cancer diagnosis. However, MRI data was only available for 14 of these 35 cancers. The following MRI analysis showed that typical breast cancer features were visible in 71% and typical benign or dubious features were seen in the remaining 29%. Of the 23 females with confirmed benign breast disease, 89 different benign breast lesions were identified. However, MRI imaging was only available for 67 lesions. Of these, 82% displayed typical benign features and 18% displayed dubious/malignant features. Those who displayed dubious/malignant features proceeded to biopsy for further clarification.

Although the study was limited by low numbers of PHTS breast cancers with available MRI data, Hoxhaj concluded that MRI should be considered as a tool for early diagnosis of breast cancer in this patient cohort and could also help to reduce the number of biopsies patients with PHTS are subject to. Whilst these findings are promising, further evaluation in larger samples is required to provide consensus. ●

## Ultrasonography Allows Detection of Vascular Complications Following Renal Transplantation

RENAL transplant is the primary treatment option for patients presenting with end-stage renal disease. In fact, not only does transplant provide a better quality of life for the patients, but it is also associated with a longer life expectancy. In this context, Doppler ultrasound is a useful tool employed to evaluate the transplanted kidney, both in the postoperative period and in the long-term follow-up, particularly for the assessment of vascular patency and the detection of complications within the renal vasculature.

At ECR 2022, Teresa Cobo Ruiz, Radiology Resident, Hospital Universitario Marqués de Valdecilla Santander, Spain, shared an insightful presentation on the potential of Doppler ultrasound in detecting vascular complications following renal transplantation. Although rare, vascular complications, which only occur in less than 10% of patients, can result in kidney loss. Therefore, being able to recognise them in a timely manner is essential.

In this review presentation, the author presented the role of ultrasonography in the detection of vascular complications.

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**"Although rare, vascular complications, which only occur in less than 10% of patients, can result in kidney loss, therefore being able to recognise them in a timely manner is essential."**

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Firstly, in segmental infarctions, contrast-enhanced ultrasound can be used to confirm the presence of these infarctions. If stenosis in the common or external iliac artery occurs, spectral Doppler ultrasound will display parvus-tardus waveforms in the main and interstitial arteries, elevated velocities at the stenosis, and downstream parvus-tardus waveforms. In renal artery stenosis, spectral Doppler ultrasound displays turbulent flow with aliasing at the stenosis and parvus-tardus waveforms in the renal arteries and renal parenchymal arteries. In renal artery thrombosis, the ultrasound shows absent arterial and venous flow distal to the thrombosed segment of the renal artery. If renal vein thrombosis occurs,



Doppler ultrasound displays enlarged kidney with absent or diminished renal flow in the main renal area and complete reversal of diastolic flow in the main renal artery and intrarenal arterial branches. In a pseudoaneurysm, anechoic image with yin–yang flow will be observed in the Doppler ultrasound. Finally, arteriovenous fistulas appear as turbulent flow or colour mosaic beyond the confines of a normal vessel on color Doppler.

This review demonstrated the usefulness and effectiveness of ultrasonography to evaluate anatomical characteristics and vascular Doppler flow in renal transplant. Cobo Ruiz concluded by highlighting that many vascular complications may be potentially treatable if detected early, and the interventional radiologist has an important therapeutic role in these cases. ●





## Dose Exposure in Common Radiological Procedures: The Patient Perspective

RADIOLOGICAL procedures, which are used widely across hospital departments around the globe, expose patients to doses of ionising radiation. Their continued use has led to a rise in the number of patients requiring reliable and adequate information about the risks such procedures can pose.

Both governments and non-governmental bodies, including the European Atomic Energy Community (EURATOM) and the International Atomic Energy Agency (IAEA), have endorsed the right to information for patients. In 2013, a EURATOM directive outlined patient knowledge about radiation doses in particular procedures, and the IAEA has affirmed that professionals must inform patients about both the potential benefits of radiological procedures, and the risks which come with exposure to ionising radiation. Countries including Italy have made it an obligation for medical professionals to give "specific and adequate information to the patient" before such procedures.

In 2013, the ESR launched the ESR Patient Advisory Group (ESR-PAG), in order to bring patients and healthcare professionals together to positively influence advances in medical imaging throughout Europe, and to improve communication between patients and healthcare departments, ultimately improving services.

At ESR 2022, study lead Sergio Salerno, Department of Biomedicine, Neuroscience Advanced Diagnosis (BIND), A.O.U.P. 'Paolo Giaccone' University of Palermo, Sicily, Italy, presented the results of a cross-sectional study in collaboration with Radiology departments at A.O.U. 'Carreggi' University of Firenze, Italy; Ospedale Pediatrico Bambino Gesù,

Rome, Italy; and Istituto 'Giannina Gaslini', Genova, Italy. Researchers aimed to investigate patients' understanding of ionising radiation in radiological procedures, patients' interest in knowing the dose of radiation they were exposed to, and what the most effective written method would be in conveying dose exposure for different patient groups.

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**"Their continued use has led to a rise in the number of patients requiring reliable and adequate information about the risks such procedures can pose."**

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Patients from all four centres were included, provided that they were undergoing planned rather than emergency radiological examinations, and their participation was voluntary. All patients (n=1,009) filled in an anonymous questionnaire. Overall, 68.1% of respondents were female; 7.1% were parents of paediatric patients.

Conclusions reached were that the majority of patients were interested in knowing exposure levels in radiological procedures, and that information presented with corresponding icons provided the most understanding across patient groups (sex, education level, and socioeconomic level). The recommendation of the researchers is that such icons should be improved, in order to ensure an "explanatory semi-quantitative model," which can be "universally understood." ●



# The Latest in Artificial Intelligence-Powered, Software-Defined MR Systems and Solutions

**Support Statement:** This content was created in partnership with Philips, based on information shared at a Philips-hosted press luncheon at ECR.

THE COVID-19 pandemic has been a catalyst for change and amplified a number of challenges in healthcare. However, one constant throughout this period has been the importance of diagnosis. Despite this, the diagnostic process has never been as complicated as it is today. At ECR 2022, which took place in Vienna, Austria, Kees Wesdorp, Chief Business Leader of Precision Diagnosis at Philips (Eindhoven, the Netherlands), and Arjen Radder, General Manager of Magnetic Resonance (MR) at Philips, discussed why Philips was uniquely positioned to drive meaningful change in this field.

According to the latest Philips Future Health Index report, one of the most substantial challenges facing radiology leaders is managing the vast quantity of data available to them. Indeed, almost one quarter of respondents cited data management as their top issue. Philips offer a suite of artificial intelligence-powered and software-defined systems that can help turn relevant data into actionable insights, leading to increased diagnostic confidence and improved clinical outcomes.

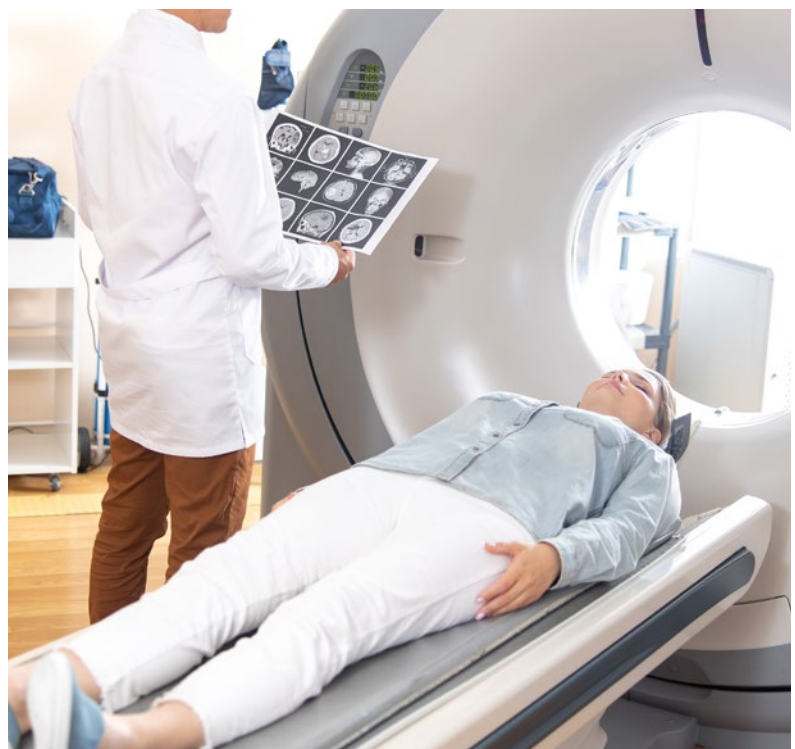
At this year's ECR, Philips introduced SmartSpeed, their latest artificial intelligence-powered, MR acceleration software, which can deliver higher image resolution with three times faster scanning times. SmartSpeed is also notable for being compatible with 97% of current clinical MR protocols, which enables faster and high-quality scans for individuals with various conditions, including those with implants. The MR 7700 was also shown at ECR 2022 for the first time. This smart, connected imaging system enhances diagnostic confidence and improves efficiency as well as patient and staff experience.

Other new innovations included the software-defined and helium-free MR 5300; the Spectral CT 7500, which is capable of delivering a 34% decrease in overall time to diagnosis; and the Philips Radiology Operations Command Center, which removes communication barriers and connects imaging experts in a command centre with technologists at scan locations across an organisation. Wesdorp shared his belief that these breakthrough solutions will bring Philips one step closer to its goal of improving 2.5 billion lives per year by 2030. ●

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**"At this year's ECR, Philips introduced SmartSpeed, their latest artificial intelligence-powered, MR acceleration software."**

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# The Role of Radiologists in Screening Programmes for Lung and Prostate Cancer

**Author:** Darcy Richards, Editorial Assistant

**Citation:** EMJ Radiol. 2022;3[1]:18-22. DOI/10.33590/emjradiol/10030701. <https://doi.org/10.33590/emjradiol/10030701>.

 DETECTING cancer at an early stage is a multi-faceted challenge for clinicians. Screening programmes aid identification of disease before symptoms arise, when prognosis is likely to be better. However, several barriers affect implementation, uptake, and delivery of these programmes. A session on the early detection and diagnosis of lung and prostate cancer, and the role of radiologists, took place at this year's hybrid European Congress of Radiology (ECR) 2022 in Vienna, Austria, 13<sup>th</sup>–17<sup>th</sup> July. The session provided expert discussion on the importance of lung and prostate cancer screening programmes; the role of radiologists in screening programme guidelines, early detection, and diagnosis; the challenges associated with population-based screening; and hopes for the future.

## **THE ROLE OF RADIOLOGISTS IN SCREENING**

Screening guidelines are a crucial element for evidence-based management. From contributing to guidelines to analysing and reporting scans, the role of the radiologist is imperative for accurate diagnosis to enable appropriate subsequent management. Caro Franck, Antwerp University Hospital (UZA), University of Antwerp, Belgium, highlighted how “lung cancer is a public health issue” and that diagnosis is often made at a late stage when curative treatment is not possible, resulting in high mortality. As an example of their role in screening programmes, Franck noted the importance of radiologists working alongside medical physicists to develop low-dose CT protocols for cancer screening and highlighted the crucial role in reading the scans.

## **THE IMPORTANCE OF EARLY DETECTION**

The experts at the ECR 2022 session agreed that early detection is key to improving outcomes for patients with lung and prostate cancer, as population-based screening programmes save lives by improving rates of cancer detection prior to metastasis.

Erik Briers, Patient Advocate, Hasselt, Belgium, and member of the European Society of Radiology (ESR) Patient Advisory Group, highlighted how risk-stratified, population-based screening can lead to early detection of prostate cancer, and that active surveillance should be standard care for those deemed low-risk following initial serum prostate-specific antigen (PSA) screening to enable prompt action if PSA rises.

Anne-Marie Baird, Trinity College, Dublin, Ireland, and President of Lung Cancer Europe (LuCE), added to this,

ECR 2022




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**"From contributing to guidelines to analysing and reporting scans, the role of the radiologist is imperative for accurate diagnosis to enable appropriate subsequent management."**

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highlighting that lung cancer accounts for almost 20% of cancer-associated mortality in Europe. Baird noted that "currently, the majority of people are diagnosed with late-stage disease," which emphasises the necessity for early screening programmes in the at-risk population to enable early diagnosis when prognosis is better.

Further to this, Briers highlighted that since free PSA testing for males >50 years in Belgium was discontinued in 2010, the number of prostate cancer diagnoses and deaths have risen. Briers stated that >50% of prostate cancers

are picked up at higher stages (Stages II–IV), rather than at early stage (Stage I). These findings highlight the value of early screening in identifying cancer at an earlier stage, for better patient outcomes across a larger group of patients.

### **BARRIERS TO SCREENING AND EARLY DIAGNOSIS**

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Lack of awareness, distance to facilities, cost and infrastructure, access, symptom normalisation, pre-conceived beliefs about screening, resource limitations, funding, and fear are some of the barriers that impede early cancer screening.

Access to hospitals or facilities limits participation in screening programmes. A UK study found that one of the main reasons to decline participation was the travel distance from their home to the hospital. One way in which this could be overcome is the use of mobile CT units. Baird highlighted how access to accurate diagnostics improves outcomes through better-informed



treatment plans, which ultimately improves quality of life for patients.

### **AWARENESS, INFRASTRUCTURE, AND FUTURE INNOVATIONS**

To improve the delivery of screening programmes, the session speakers noted a need to increase awareness of cancer screening programmes. Briers highlighted that “awareness of prostate cancer is extremely important; prostate cancer is something that you need to know about to be motivated to go for a very simple screening test;” while Baird stated that “there is a lack of public

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**"Early detection is key to improving outcomes for patients with lung and prostate cancer, as population-based screening programmes save lives."**

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awareness” surrounding lung cancer screening.

Franck discussed how data from existing screening programmes and epidemiological studies have shown the benefit of low-dose CT screening in those deemed at high-risk for lung cancer. The NLST (USA) and the NELSON (Belgium and the Netherlands) trials have both shown “a reduction in lung cancer-specific mortality with low-dose CT.” Other European trials such as LUSI (Germany), MILD (Italy), and UKLS (UK) have shown similar results. Despite this evidence, uptake into screening programmes is low. Franck stated that one way in which this could be improved is for radiologists to have “a more visible role” in public education on imaging-based cancer screening.

One of the concerns considered with imaging-based screening programmes is exposure to radiation through imaging techniques. Franck highlighted the role of medical physicists and radiologists in developing low-dose CT protocols for lung cancer screening to balance





achieving optimal image quality with the lowest dose of radiation possible. This prevents the need for repeat scans secondary to poor image quality, reducing radiation exposure and risk of radiation-induced malignancy.

Franck spotlighted further innovations, including how the use of artificial intelligence-based computer-aided detection (CAD) software could revolutionise reading of lung cancer screening images. Upon the CAD of a nodule, the scan would be forwarded to a radiologist for verification; however, if there is no CAD of a nodule, no further action would be required. This could greatly reduce the increased workload that an imaging-based screening programme roll-out would generate for radiologists.

Looking forward, the 'Europe's Beating Cancer Plan' has been announced. There is hope that this will include screening programme outlines for multiple different cancers, including lung and prostate cancers, and provide a roadmap to facilitate roll-out across different member states.

### **PANEL DISCUSSION: QUESTIONS FOR THE EXPERTS**

#### **How Do False Negatives from Serum Prostate Specific Antigen Affect Screening?**

Briers noted that there were "very few" false negatives; however, certain subtypes of prostate cancer, such as neuro-endocrine prostate cancer, do

not cause elevated PSA and, therefore, patients can have low PSA levels despite metastasised cancer. This highlights that although screening aims to improve detection rates and, ultimately, patient outcome, it will not catch all prostate cancers.

#### **Was Cost Considered When Analysing Priority Settings and Resource Limitations in Research Conducted by Lung Cancer Europe?**

Baird shared that cost-effectiveness was not included in the questionnaire as it was targeting those living with the disease or in a care-giving capacity and their understanding of lung cancer screening. Baird commented that, as given screening is for those who are at high-risk but asymptomatic, these patients would likely accept delays in access because of the comfort in being involved in a screening programme where patients are being monitored.

#### **How Can Infrastructure Be Improved to Increase the Pace of Screening and Patient Prioritisation?**

The experts discussed how hospitals would need to recruit additional radiologists to read the scans from lung cancer screenings and re-emphasised the potential role for CAD to reduce the burden of scans to review by clearing the negative scans. Franck highlighted how resource requirement calculators can help plan accurate and adequate resource distribution.

Briers noted that to detect and curatively treat early-stage prostate cancer costs approximately 10,000 EUR; however, to treat metastasised prostate cancer the cost can range 200,000–500,000 EUR per patient. This should be considered in the cost evaluation for screening programmes. Briers further added that not every patient will be invited to imaging and not all those invited will attend. For

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**"Ensuring adequate awareness, infrastructure, and accessibility will be key in implementing these necessary programmes."**

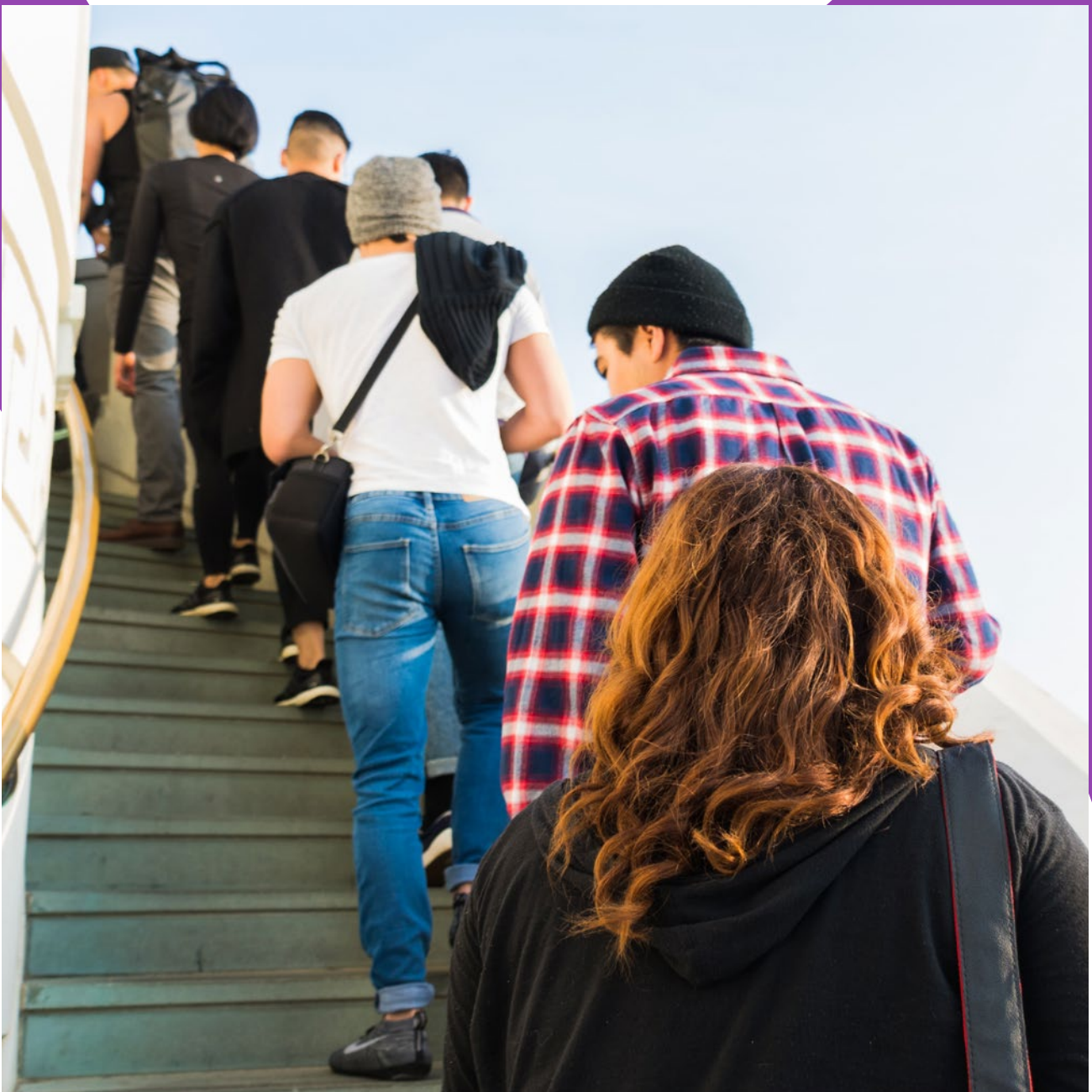
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prostate cancer, only individuals with a PSA above a certain cut-off should be included at initial screening; for lung cancer screening, it should be those deemed high risk (e.g., those with a heavy smoking history).

## **CONCLUSION**

This ECR 2022 session highlighted the key role of radiologists in improving early cancer detection via screening programmes. Expert input from multidisciplinary professionals

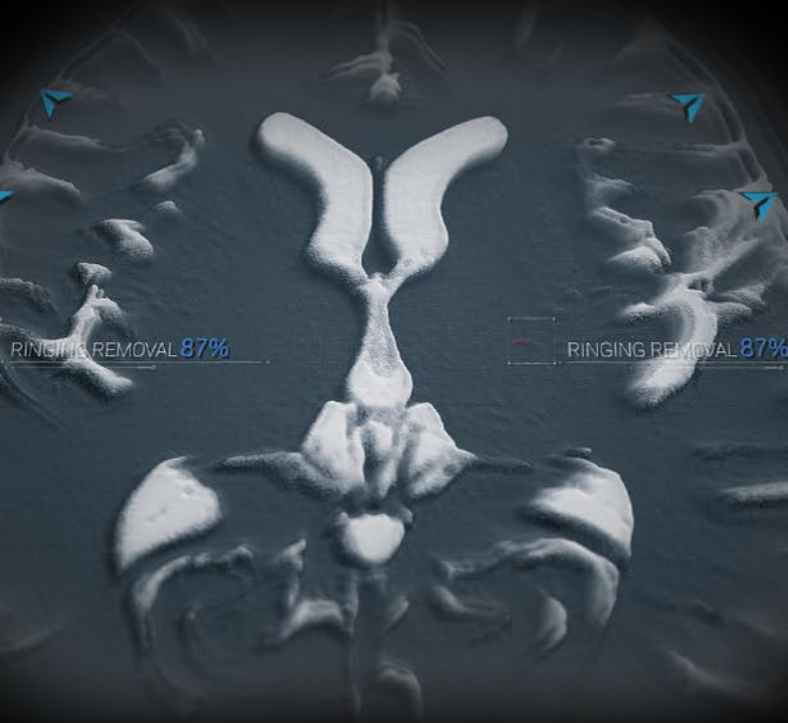
to develop effective screening programmes for early cancer detection is imperative to improving public health. Ensuring adequate awareness, infrastructure, and accessibility will be key in implementing these necessary programmes. With advances in radiology, artificial intelligence, and patient advocacy, and in light of Europe's Beating Cancer Plan, rates of early detection and diagnosis could increase to ultimately provide treatment at earlier stages, when prognosis is better. ●





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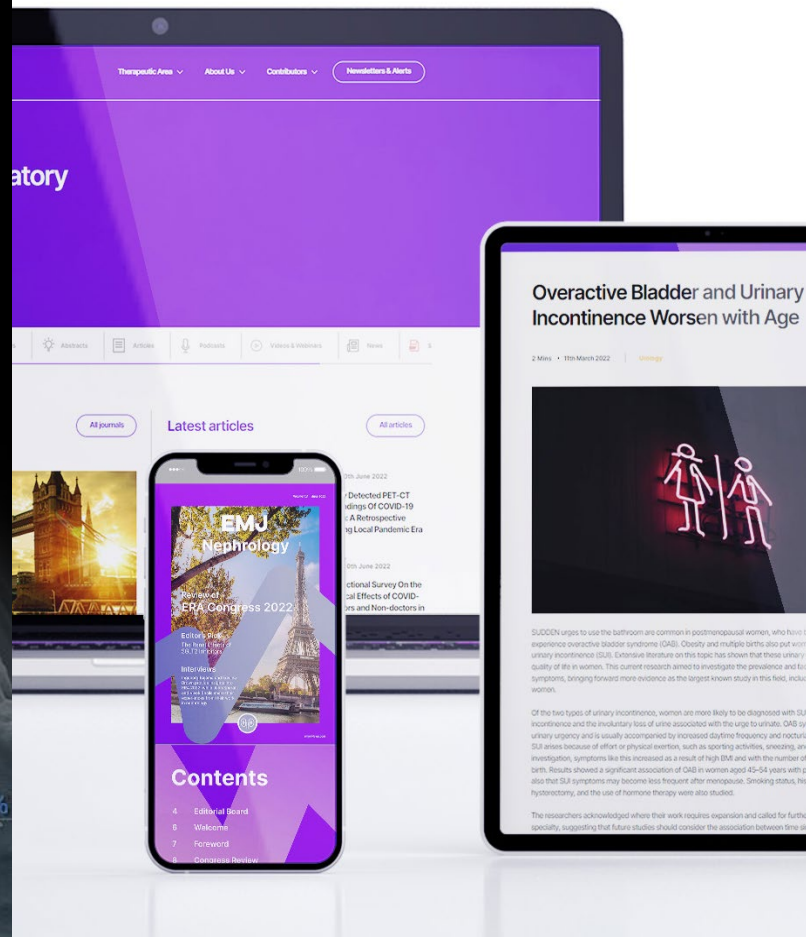
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# Abstract Reviews

Introducing the latest research in the field of radiology presented at the European Congress of Radiology (ECR) 2022.

## Radiologic–Pathologic Correlation in 1-Year Follow-Up After COVID-19 Infection

**Authors:** \*Diletta Cozzi,<sup>1</sup> Edoardo Cavigli,<sup>1</sup> Silvia Luvarà,<sup>1</sup> Alessandra Bindi,<sup>1</sup> Chiara Moroni,<sup>1</sup> Sara Tomassetti,<sup>2,3</sup> Valeria Pasini,<sup>4</sup> Camilla Eva Comin,<sup>4</sup> Vittorio Miele<sup>1</sup>

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**Disclosure:** The authors have declared no conflicts of interest.

**Keywords:** Biopsy, COVID-19, high-resolution chest CT (HRCT), interstitial lung disease.

**Citation:** *EMJ Radiol.* 2022;3[1]:24–26. DOI/10.33590/emjradiol/10000521. <https://doi.org/10.33590/emjradiol/10000521>.

### BACKGROUND AND AIMS

The severe acute respiratory syndrome coronavirus 2 pandemic has already infected millions of people worldwide, with 5–10% of cases leading to severe pneumonia. Although the majority improve over time, some patients may progress to post-COVID-19 interstitial lung disease. The aim of this abstract review was to investigate the characteristics of post-COVID-19 interstitial lung changes, with the unique

opportunity to evaluate radiologic–pathologic correlations using high-resolution chest CT (HRCT) and transbronchial lung cryobiopsy specimens.

### MATERIALS AND METHODS

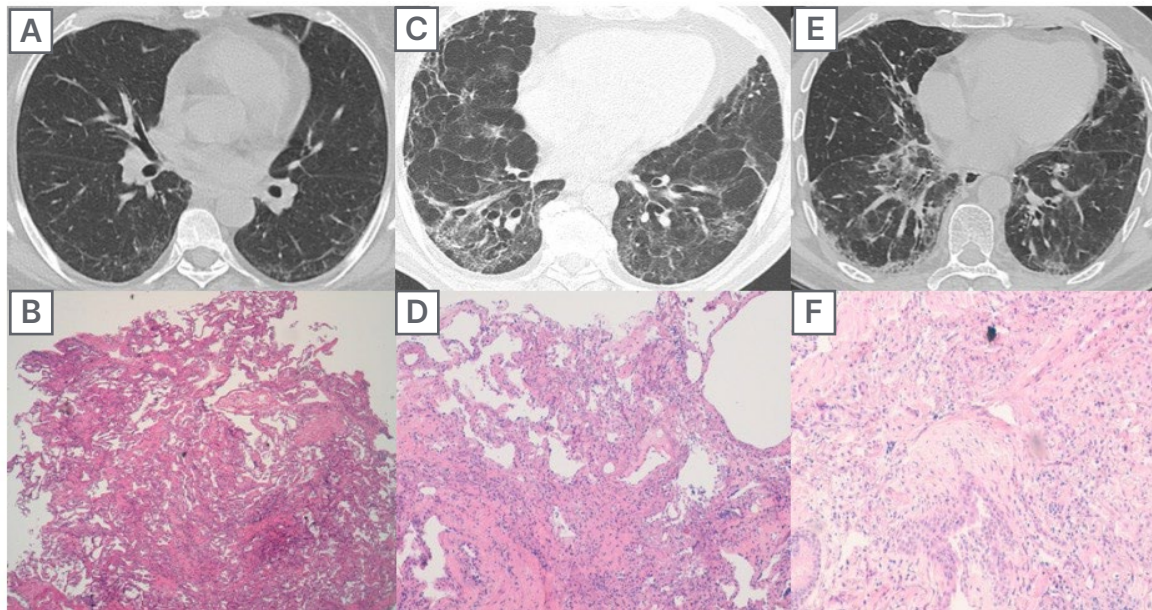
The authors used preliminary results of HRCT features of post-COVID-19 interstitial lung disease. The authors collected data of hospitalised patients at baseline, then at 6 ( $\pm 1$ ) months and 12 ( $\pm 1$ ) months after discharge. HRCT changes at 6 months involving more than 5% of the total lung volume were considered significant, following the current definition of interstitial lung abnormalities. Thoracic radiologists were asked to define each HRCT as negative for pleural and parenchymal alterations, or if positive, whether alterations were predominantly fibrosing-like or non-fibrosing-like. Patients with significant HRCT changes underwent bronchoalveolar lavage and/or cryobiopsy, and a subsequent follow-up with HRCT and lung function evaluation at 18 ( $\pm 1$ ) months.

### RESULTS

At the time of the present interim analysis, 139 patients from the Careggi University Hospital, Florence, Italy, were enrolled. Median age was 67 years (range: 18–87 years), and 85 were males (61.1%). At 12-month follow-up, HRCT significant changes (both fibrotic-like and non-fibrotic-like) were detected in 53 subjects (38.1%). Of these, only 2/53 (3.8%) patients had parenchymal progression of the disease. There was stability in 33/53 (62.3%) and improvement of lung involvement in 18/53 (33.9%). Cryobiopsies were performed in 10 patients, showing some discordance with radiological appearance



Figure 1: 12-month follow-up high-resolution chest CT and correlation with histology.



**Case 1 (A-B):** HRCT 12-month follow-up with an indeterminate-pattern fibrosis. **(A)** Biopsy specimen shows homogeneous septal thickening with initial fibrosis and dilatation of the interstitial capillaries. Initial inflammatory infiltrate in the peribronchiolar area, classified as indeterminate fibrosis. **(B)** In this case, multidisciplinary decision was post-COVID-19-related fibrosis. **Case 2 (C-D):** 12-month follow-up HRCT with a fibrosing NSIP/OP pattern and diffuse bronchial distortion. **(C)** Histological evaluation demonstrates the presence of dense and diffuse fibrosis, mild interstitial inflammation, with prominent bronchiolar damage (epithelial damage including epithelial detachment and alveolar denudation). **(D)** This is a case of ventilator-associated lung injury. **Case 3 (E-F):** HRCT with a probable UIP pattern. **(E)** Confirmed also with the biopsy showing dense patchy fibrosis with microscopic honeycombing and a fibroblastic foci. **(F)** Multidisciplinary decision was pulmonary fibrosis, and the patient started antifibrotic therapy.

HRCT: high-resolution chest CT; NSIP: non-specific interstitial pneumonia; OP: organising pneumonia; UIP: usual interstitial pneumonia.

(Figure 1). In particular, biopsy found two cases of histological usual interstitial pneumonia (UIP)/early UIP, where HRCT demonstrated a non-specific interstitial pneumonia (NSIP)/organising pneumonia (OP) pattern. Cryobiopsy confirmed one case of HRCT UIP-probable pattern, and three cases of NSIP/OP/hypersensitivity pneumonitis pattern. Moreover, histological evaluation confirmed the radiological pattern found in two cases of early fibrosing disease related to COVID-19 infection, and in two cases of fibrosing ventilator-associated lung injury.

## CONCLUSION

This preliminary analysis confirmed that after COVID-19 infection, a minority of patients developed interstitial lung changes, mostly with an NSIP/OP or (early) UIP pattern. The UIP pattern found in this study could be the expression of a pre-existing non-diagnosed lung fibrosis or idiopathic pulmonary fibrosis. The hypothesis is that the infection could be a trigger for a possible underlying latent interstitial disease in predisposed subjects.

## LIMITATIONS

This study used a small sample size of patients with fibrotic-like changes (without histologic

confirmation), which may need a longer follow-up to determine whether the fibrotic-like changes are permanent, progressive, or reversible. ●

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## Early Diffusion-Weighted MRI at 3 Tesla Detects Ischaemic Changes of the Optic Nerve in Anterior Ischaemic Optic Neuropathy

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**Disclosure:** The authors have declared no conflicts of interest.

**Keywords:** Diffusion MRI, ischaemic, MRI, optic neuropathy.

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### BACKGROUND AND AIMS

Anterior ischaemic optic neuropathy (AION) is the most common acute optic neuropathy in older patients. Its annual incidence is 2.3–10.2 cases per 100,000 persons over 50 years. AION can be classified into non-arteritic, accounting for 95% of AION cases, and arteritic, which is mainly associated with giant cells arteritis. Early and accurate diagnosis is essential to avoid severe and irreversible complications such as permanent visual loss.<sup>1</sup>

The objective of the authors' study was to assess the impact of timing from onset of visual symptoms to diffusion-weighted 3 Tesla (T) MRI completion to detect ischaemic changes of the optic disc and optic nerve in patients with AION.

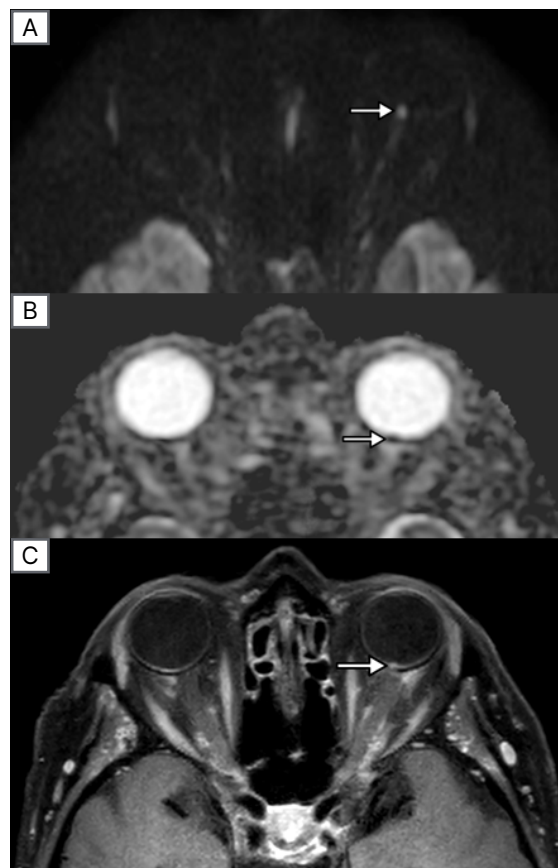
### MATERIALS AND METHODS

This institutional review board-approved retrospective single-centre study included 3T MRI data from 126 patients with AION and 111 controls with optic neuritis, who were treated between January 2015 and May 2020. Two radiologists, blind to all data, individually analysed imaging. A senior neuroradiologist resolved any discrepancies by consensus. The primary judgment criterion was the restricted diffusion of the optic disc and/or the optic nerve assessed subjectively on the apparent diffusion coefficient (ADC) maps. ADC values were also measured. Spearman's rank correlation coefficients were used to examine the relationships between timing from onset of visual symptoms to MRI completion, and both the restricted diffusion and the ADC values.

### RESULTS

A total of 126 patients (47 [37.3%] were females and 79 [62.7%] were males; mean age: 69.1±13.7 years) with AION were included. Restricted diffusion of the optic disc in eyes with AION was more frequent in the early MRI group than in the late MRI group (35 out of 49 [71.4%] eyes versus three out of 83 [3.6%] eyes, respectively;  $p < 0.001$  [Figure 1]). ADC values of the pathological optic discs and optic nerves were lower in the early MRI group than in the late

**Figure 1: MRI of an 86-year-old female presenting to the emergency department for acute visual loss of the left eye.**



MRI was performed 3 days after the onset of visual symptoms. In the left optic disc (arrow), diffusion-weighted MRI **(A)** shows high signal intensity and ADC map **(B)** shows reduced ADC value as sign of restricted diffusion. Post-contrast T1-weighted imaging **(C)** shows enhancement of the left optic disc (arrow). A diagnosis of arteritic anterior ischaemic optic neuropathy of the left eye was confirmed.

ADC: apparent diffusion coefficient; T: tesla.

MRI group ( $0.61 [0.52-0.94] \times 10^{-3} \text{ mm}^2/\text{s}$  versus  $1.28 [1.01-1.44] \times 10^{-3} \text{ mm}^2/\text{s}$ ;  $p < 0.001$  and  $0.74 [0.61-0.88] \times 10^{-3} \text{ mm}^2/\text{s}$  versus  $0.89 [0.72-1.10] \times 10^{-3} \text{ mm}^2/\text{s}$ ;  $p < 0.001$ , respectively).

To the best of the authors' knowledge, this study was the first one to show a correlation between successfully detecting ischaemic changes in AION and the timing from the onset of AION to the completion of MRI.<sup>2</sup> Restricted diffusion of the optic disc was observed in the majority of eyes with AION in the early MRI group, but only rarely in the late MRI group. The authors showed that a threshold of 5 days was optimal to detect ischaemic changes of the optic disc or optic

nerve in AION. It highlights the need to perform an MRI as soon as possible to be able to detect ischaemic changes of the optic disc or optic nerve in patients with a suspected diagnosis of AION.

Based on the authors' results, although a simple visual evaluation of ADC map might be challenging and subjective, an ADC measurement should be systematically performed to confirm a restricted diffusion of the optic nerve or optic disc. Based on the authors' receiver operating characteristic curves, they provided an optimal ADC threshold of 0.63 for the optic disc to detect AION, yielding a specificity of 95%. This



threshold might be used easily in clinical practice.

## CONCLUSION

The authors' results have the potential to modify the management of patients with a suspected diagnosis of AION. Fast-track pathways, including emergency access to an MRI examination, should be considered for diagnosing patients with a suspected diagnosis of AION.<sup>3-5</sup>

In conclusion, diffusion-weighted MRI showed good diagnostic performance to detect AION when performed early after the onset of visual symptoms. ●

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# Dual-Energy CT as an Adjunct to Evaluate the Significance of Type II Endoleaks After Endovascular Aneurysm Repair

**Authors:** \*Stavros Charalambous,<sup>1,2,3</sup> Kostas Perisinakis,<sup>4</sup> Nikolaos Kontopodis,<sup>5</sup> Antonios E. Papadakis,<sup>4</sup> Giorgos Prekatsounis,<sup>2</sup> Thomas G. Maris,<sup>4</sup> Christos V. Ioannou,<sup>5</sup> Apostolos Karantanas,<sup>1,2</sup> Dimitrios Tsetis<sup>1,2,3</sup>

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**Disclosure:** The authors have declared no conflicts of interest.

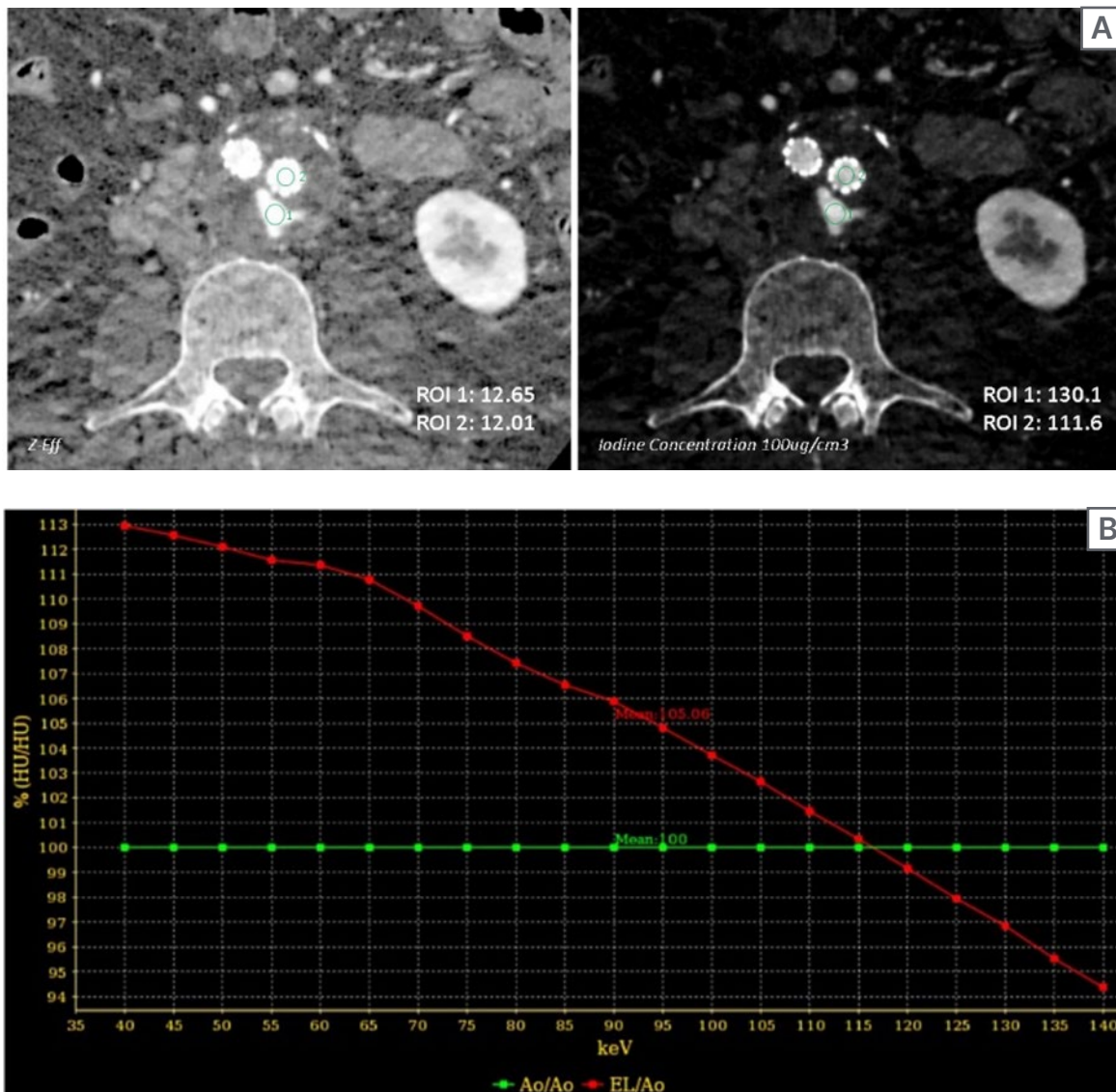
**Keywords:** Aortic aneurysm, CT, dual-energy CT, endoleak, endovascular repair.

**Citation:** *EMJ Radiol*. 2022;3[1]:28-31. DOI/10.33590/emjradiol/10100234. <https://doi.org/10.33590/emjradiol/10100234>.

## BACKGROUND AND AIMS

Endoleak is the drawback of endovascular aneurysm repair (EVAR), and is defined as the continued blood flow inside the remnant abdominal aortic aneurysm (AAA) sac despite stent-graft deployment.<sup>1</sup> CT angiography is the gold standard imaging modality for endoleak detection after EVAR.<sup>2</sup> Among five types described, Type II endoleak (T2EL) is by far the most common but its clinical effects after diagnosis remain controversial. Most T2ELs usually follow a benign course and resolve spontaneously within 6 months.<sup>3</sup> On the contrary, persistent T2ELs require lifelong imaging surveillance to assess their impact on the AAA sac size. To the best of the authors' knowledge, the exploitation of data derived from dual-energy CT imaging for predicting the evolution of T2EL after EVAR has not been previously investigated. The aim of this study was to investigate the value of dual-energy CT imaging as an adjunct to discriminate aggressive from benign T2EL after EVAR.

Figure 1: A)  $Z_{\text{eff}}$  and IC axial images are illustrated. B)  $HU_{\text{endoleak}}/HU_{\text{aorta}}$  against monochromatic energy is illustrated.



A) ROIs were placed on endoleak (ROI 1) and within aorta (ROI 2) to obtain the NIC and  $NZ_{\text{eff}}$  for T2EL.  
 B) S, DEI, and an improvised parameter, EI, were calculated.

Ao: aorta; DEI: dual energy index; EI: endoleak index; EL: endoleak; HU: Hounsfield unit; IC: iodine concentration; NIC: normalised iodine concentration;  $NZ_{\text{eff}}$ : normalised effective atomic number; ROI: region of interest; S: slope; T2EL: Type II endoleak;  $Z_{\text{eff}}$ : effective atomic number.

## MATERIALS AND METHODS

Study participants were consecutive patients referred for CT at 1 month after EVAR. CT imaging acquisition included a dual-energy CT angiography (DECTA) and a delayed single-energy CT (SECT) imaging. Patients diagnosed with T2EL were re-examined at 6 months post-EVAR to assess the aneurysm sac growth (ASG)

through  $ASG = D6 - D1$ , where D1 and D6 represent the maximum AAA sac diameter at 1 month and 6 months CT imaging, respectively. Upon ASG recorded, patients were categorised as having benign (Group A) or suspicious for aggressive (Group B) T2EL.

DECTA image data (Figure 1) were employed to calculate five parameters: the normalised

Figure 2: Parameters calculated with DECTA imaging data.

$$\begin{aligned}
 \text{2A)} \quad NZ_{\text{eff}} &= \frac{(Z_{\text{eff}})_{\text{endoleak}}}{(Z_{\text{eff}})_{\text{aorta}}} & \text{2B)} \quad \text{NIC} &= \frac{IC_{\text{endoleak}}}{IC_{\text{aorta}}} \\
 \text{2C)} \quad S &= \frac{(HU)_{\text{endoleak}} / (HU)_{\text{aorta}} \text{ at lowkeV} - (HU)_{\text{endoleak}} / (HU)_{\text{aorta}} \text{ at highkeV}}{(\text{highkeV} - \text{lowkeV})} \\
 \text{2D)} \quad \text{DEI} &= \frac{HU_{\text{endoleak}}^{\text{lowkeV}} - HU_{\text{endoleak}}^{\text{highkeV}}}{HU_{\text{endoleak}}^{\text{lowkeV}} + HU_{\text{endoleak}}^{\text{highkeV}} + 2000} \\
 \text{2E)} \quad \text{EI} &= \frac{(HU)_{\text{endoleak}} / (HU)_{\text{aorta}} \text{ at lowkeV} + (HU)_{\text{endoleak}} / (HU)_{\text{aorta}} \text{ at highkeV}}{(HU)_{\text{endoleak}} / (HU)_{\text{aorta}} \text{ at lowkeV} + (HU)_{\text{endoleak}} / (HU)_{\text{aorta}} \text{ at highkeV}}
 \end{aligned}$$

DEI: dual-energy index; EI: endoleak index; HU: Hounsfield unit; IC: iodine concentration; NIC: normalised iodine concentration;  $NZ_{\text{eff}}$ : normalised effective atomic number; S: slope;  $Z_{\text{eff}}$ : effective atomic number.

effective atomic number ( $NZ_{\text{eff}}$ ), through Figure 2A; the normalised iodine concentration (NIC), through Figure 2B; the slope (S) of Hounsfield unit (HU)  $(HU)_{\text{endoleak}} / (HU)_{\text{aorta}}$  against monochromatic energy, through Figure 2C; the dual-energy index (DEI), through Figure 2D; and an improvised endoleak index (EI), through Figure 2E for each T2EL. Statistical analysis was employed to compare all above parameters regarding their ability to differentiate aggressive from benign T2EL. The sum of three SECT imaging acquisitions commonly involved in follow-up CT examinations of EVAR patients was compared regarding patient radiation burden to a CT examination comprised by a DECTA and a delayed SECT.

## RESULTS

Among 40 patients examined at 1 month after EVAR, 14 patients (35%) were diagnosed with T2EL. Among the 14 patients diagnosed with T2EL, nine patients were assigned to Group A,

and five patients were assigned to Group B.  $NZ_{\text{eff}}$  and EI were found to be significantly lower in Group A than in Group B ( $p < 0.05$ ). There were no significant differences in NIC, DEI, and S values between Groups A and B ( $p > 0.05$ ).  $NZ_{\text{eff}}$  was found to have the highest power to discriminate aggressive T2EL with an area under the curve of 86.7%, showing 100% specificity and 60% sensitivity. Similarly, EI showed an area under the curve of 84.4%, specificity of 100%, and sensitivity of 60%. The mean effective dose from DECTA and SECT scans was 27.8% lower compared with the corresponding cumulative dose from the commonly employed imaging scenario that includes three SECT acquisitions (27.06 versus 37.47 mSv, respectively).

## CONCLUSION

In conclusion, the use of DECT imaging at 1 month after EVAR may provide quantitative indices able to discriminate aggressive from benign T2ELs after EVAR, and could therefore



provide decision support tools to assist in patient management. ●

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# Quantification of Enhancement Intensity and Pattern of Benign and Malignant Lesions in Contrast-Enhanced Spectral Mammography and Its Correlation with MRI Enhancement Patterns

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**Keywords:** Contrast-enhanced spectral mammography (CESM), contrast-to-noise ratio (CNR), enhancement intensity, quantification, MRI, relative signal difference (RSD).

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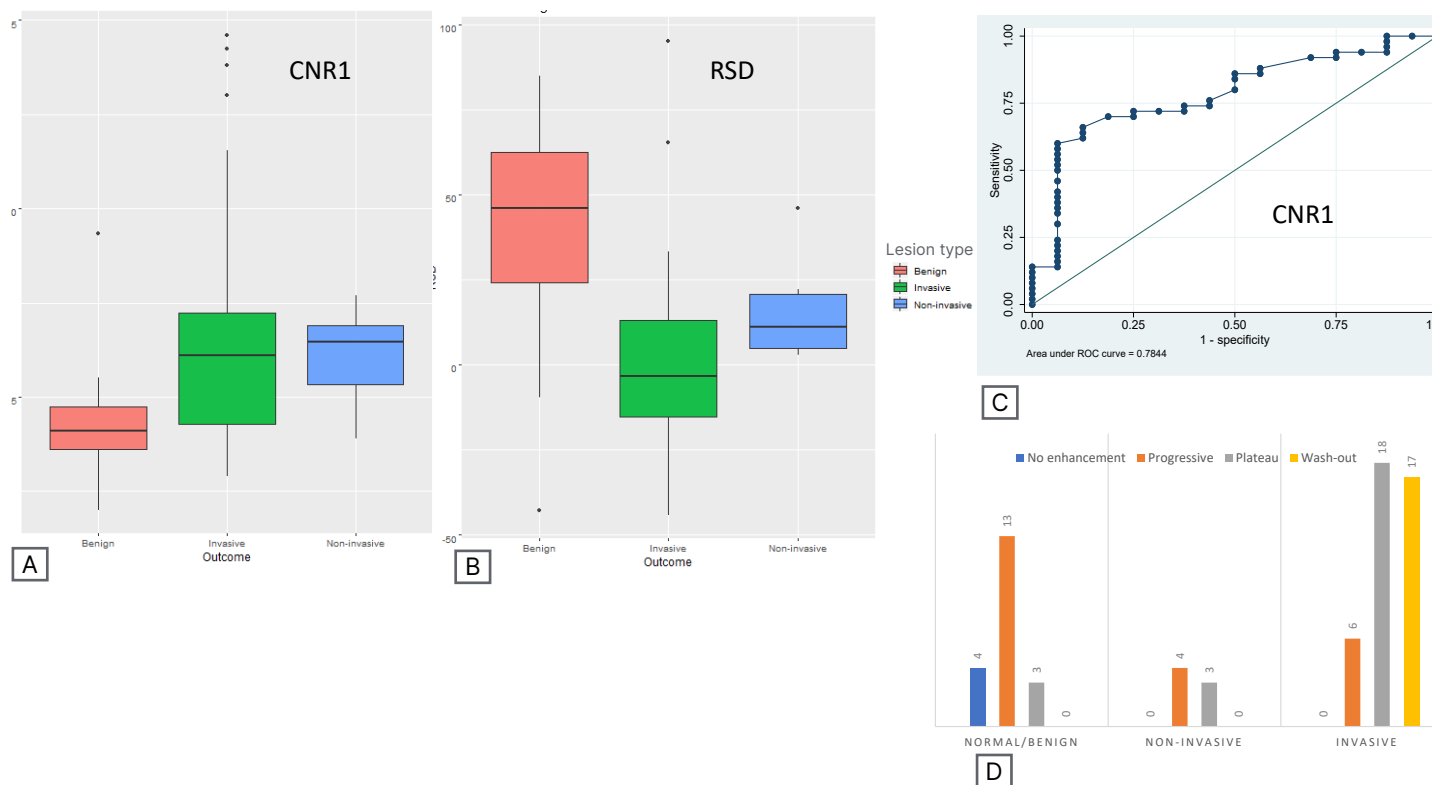
## BACKGROUND AND AIMS

Contrast-enhanced spectral mammography (CESM) is an emerging diagnostic imaging technique with a high breast cancer detection rate but limited diagnostic specificity.<sup>1</sup> Published studies have proven that CESM has similar accuracy to MRI for the detection of breast cancer, and can also give information about lesion vascularity and dynamics.<sup>1,2</sup> Therefore, quantification of lesion enhancement intensity and pattern might be helpful in increasing specificity and predicting tumour histology.<sup>1-3</sup> In this study, the authors aimed to quantify the enhancement intensity and pattern of different breast lesions seen in CESM, and to investigate the correlation with enhancement types in breast MRI.

## MATERIALS AND METHODS

Using CESM studies from the CONTENTD<sup>4</sup> and BRAID<sup>5</sup> trials, three experienced breast radiologists calculated contrast-to-noise ratio (CNR) for each lesion identified in the temporally earlier (craniocaudal view; CNR1) and later (mediolateral oblique view; CNR2), where  $CNR = \frac{Sa - Sb}{Sb}$  (Sa: maximum pixel value in breast lesion; Sb: mean pixel value of background). Relative signal difference (RSD) was calculated as  $\frac{CNR2 - CNR1}{CNR1} \times 100\%$ . Enhancement patterns in CESM were classified as no enhancement, progressive ( $RSD > 10\%$ ), plateau ( $-10\% \leq RSD \leq 10\%$ ), or washout ( $RSD < -10\%$ ). Similarly, MRI enhancement patterns were recorded for 38 lesions that had a clinical breast MRI at the same episode. The statistical analysis was conducted using Stata 17.0 (StataCorp LLC, College Station, Texas, USA). To compare groups, a Mann-Whitney U test was used for two independent

Figure 1: Diagnostic performance of CNR1 compared with RSD and enhancement patterns for benign and malignant lesions on CESM.



**A)** CNR1 and **B)** RSD values for benign, invasive, and non-invasive tumoral lesions. **C)** Diagnostic performance for CNR1. **D)** Distribution of enhancement patterns in CESM.

CESM: contrast-enhanced spectral mammography; CNR: contrast to noise ratio; ROC: receiver operating characteristics; RSD: relative signal difference.

groups, and a Kruskal–Wallis test for more than two independent groups. A p value <0.05 was deemed significant. Receiver operating characteristics curve and area under the curve were generated to assess the diagnostic performances. The study population consisted of 256 CESM research studies, from which 98 lesions were identified. Twenty-eight lesions were excluded due to suboptimal image quality or lesion seen on only one view.

## RESULTS

Histopathology of 70 lesions (3–110 mm) was 49 cancers (42 invasive, 7 non-invasive) and 21 normal/benign (seven B1, 12 B2, and two B3). The authors grouped the lesions according to their submolecular types and hormone receptor

status. The CNR1 values were significantly lower for benign lesions than for invasive cancers (mean CNR1: 0.046 versus 0.066;  $p < 0.0095$ ), but not significantly different for the non-invasive group (mean CNR1: 0.046 versus 0.058;  $p < 0.07$ ) (Figure 1A). Also, benign lesions had higher RSD values compared with malignant ones (mean RSD: 29.89 versus -8.48;  $p < 0.0001$ ) (Figure 1B). The diagnostic performance of CNR1 was better compared with CNR2 and RSD, with an area under the receiver operating characteristic curve of 0.78 (Figure 1C). The authors did not find significant values for different molecular subtypes, but this was probably related to the low number of lesions in this study. Most of the benign lesions showed progressive enhancement in CESM, while the invasive cancers' enhancement patterns were mainly washout and plateau (Figure 1D). Full agreement

between CESM and MRI enhancement patterns was found in 29 of 38 cases (76.3%), with a Pearson chi-square value  $\chi^2=54.5$  and a Cramér's  $V \varphi_c=0.69$ , showing good correlation between the two techniques.

## CONCLUSION

These preliminary results indicate that quantification of enhancement intensity in CESM may be helpful to differentiate between benign and malignant breast lesions. Furthermore, there seems to be good correlation between MRI and CESM enhancement patterns. This study was limited by the small number of pathologies. Next steps should include a larger, more heterogeneous study population; further analysis according to molecular subtypes; and possible integration of radiomic features to predict tumor histology and prognosis. ●

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# Interview



## **Fred T. Lee Jr.**

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### **Q1** With your experience in radiology and biomedical imaging, what initially sparked your interest in cancer imaging and interventions?

Having two parents who were diagnosed with cancer during my medical school years sparked my initial interest in the imaging of cancer. Our family had to live with the difficult trade-offs that all cancer patients need to make, and this got me thinking about less invasive and more effective methods to diagnose and treat cancer.

### **Q2** Your work to date has shifted to have a particular emphasis on percutaneous tumour ablation. As an early pioneer in this field, is there a particular event or person that encouraged you to go down this path?

My father was an early pioneer in the imaging and minimally invasive therapy of prostate cancer. He even diagnosed himself, and then decided to devote his remaining life to understanding and treating prostate cancer. In fact, for those of you out there who practise prostate MRI, he was the one that described the zonal anatomy of the prostate, was the first to use the prostate-specific antigen test in clinical practice, described prostate-specific

antigen density, and was one of two people (Gary Onik being the other) to drive percutaneous cryoablation as a therapy for prostate cancer. After I joined the faculty at the University of Wisconsin, USA, in 1991, he would come to my lab, and we would perform animal studies together to try and understand ablation better. I knew that the prostate was not an organ that I wanted to spend a career working on, and so applied many of the lessons that he taught me to the liver, kidney, and lungs.

### **Q3** You initially studied at Boston University, Massachusetts, USA, then moved for your residency at the University of Rochester, New York, USA, and carried out your internship at the University of Massachusetts, USA. Where do you believe that you gained the most experience, and which had the largest impact on your subsequent career?

Looking back at my training, it was never about the 'where,' but more about the 'who.' I feel fortunate to have stumbled upon mentors that didn't just teach me radiology, but rather how to approach problems, how to form and test a hypothesis, how to write, and, maybe most importantly, how to not give up in the face of seemingly

insurmountable problems. For example, Jack Thornbury and Rick Katzberg (unfortunately both deceased) taught me the beauty of academic medicine, and Rob Lerner and Stan Weiss taught me the power of cross-sectional imaging, particularly ultrasound, as a method to place needles and devices. Another hugely motivating factor in my training was my residency classmates: Jim Bronson, Bevan Bastian, Jamey Schuster, and Dana Zacharewicz. I couldn't have asked for better partners; we worked really hard together and encouraged each other. Medical training is tough, and if you don't have great people around you sharing the journey, it's easy to become discouraged and cynical.

#### **Q4** Do you think there are any misconceptions or challenges that the speciality of cancer imaging and intervention must overcome?

The entire concept of interventional oncology is fairly new, and I think we still struggle to be accepted on equal footing with medical, surgical, and radiation oncologists. I find this ironic because it is becoming increasingly obvious that image-guided therapies are here to stay, and will become more and more important to a wider segment of cancer patients as our techniques and devices become less invasive and more effective. As I look back at the last few decades, our progress is spectacular, particularly given the relatively short amount of time and small amount of funding we have received for our discoveries. For example, if one were to think about the total amount of dollars that have been spent on chemotherapies in the last two decades, if even a fraction of that amount had been applied to interventional oncology therapies, we would be in a very different place than we are today.

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**"It is becoming increasingly obvious that image-guided therapies are here to stay, and will become more and more important to a wider segment of cancer patients as our techniques and devices become less invasive and more effective."**

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**"Podcasts are one of my favourite methods to both communicate my own thoughts and hear about the work of others."**

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**Q5** How do you believe your work as a founding member of the International Working Group for Tumour Ablation has impacted patients' quality of treatment and quality of life?

The International Working Group was founded primarily by Nahum Goldberg, Damian Dupuy, and Luigi Solbiati in the early 1990s from a small group of us that were working in tumour ablation. We would meet at Gino's Pizzeria during our time at the Radiological Society of North America (RSNA) and discuss every aspect of tumour ablation, including some of the hard things like complications and suboptimal results. In some ways, because there were so few of us performing tumour ablation at that time, it initially functioned as more of a support group than a scientific forum. Nahum was interested in finding a way to expand the impact of that initial small group, and so he started to champion tangible steps to push the field further along. For example, the original tumour ablation lexicon published in Radiology standardised how we talk about tumour ablation and was a by-product of the working group. Other important documents have since come out of the working group (or a subset of it) that have established standards and expectations for the practice of tumour ablation.

**Q6** As an author whose work has resulted in over 200 scientific publications, where can we expect to see your focus lie in the coming years?

Over the past several years, I have mostly been working on histotripsy, a non-invasive, non-thermal, non-ionising

method of tissue destruction that was invented at the University of Michigan, Ann Arbor, USA approximately a decade ago. The technology is very interesting to me because of the robotic control and automation used (we need more reproducibility and standardisation in interventional oncology), the high degree of precision, the ability to destroy virtually any size and shape of tumour, and the potential post-treatment immune effects. There's a lot of work yet to be done, but the promise of better, faster, more automated, and less-invasive treatments make the effort worthwhile.

**Q7** You have been featured in podcasts such as 'The Kinked Wire', where you spoke about the potential for histotripsy in cancer treatment. How do you think working in science communication helps to contribute to collective expertise and engagement?

In the early days of my career, science communication was simple: there were peer-reviewed journals, scientific meetings, and sometimes the print version of a specialty newspaper, such as this one. As they are highly curated and accurate, these modes of communication remain important, but they lack the ability to rapidly communicate with large numbers of physicians in a medium that they use daily. I personally don't engage with social media, but can understand why some of my younger colleagues find it exceedingly useful and topical. Podcasts are one of my favourite methods to both communicate my own thoughts and hear about the work of others. There's something about hearing the author explain their thought process in-depth that I find particularly valuable, and sometimes lacking from the more traditional modes of communication.

**Q8** In 1995, when you established the tumour ablation laboratory at the University of Wisconsin, which



**was one of the first of its kind, what were the biggest challenges for the lab in achieving its initial goals?**

Tumour ablation is particularly challenging to study in humans because we rely on imperfect imaging surrogates to determine the success or failure of treatment. In contrast, surgery has the advantage of a pathologic specimen to examine margins, microscopic pathology, genetic markers, etc. My initial purpose in establishing an animal laboratory to study ablation was to

answer the simple but fundamental question: "How do you know you are doing what you think you are?" An animal lab therefore became a necessity in order to have access to tissue specimens after treatment and to correlate pathologic findings with imaging. It was a novel idea for its time, and grant funding was difficult because few reviewers had even heard of tumour ablation. For some reason, it seemed as though basic scientists with expertise in radiotherapy were the reviewers on



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**"Tumour ablation is particularly challenging to study in humans because we rely on imperfect imaging surrogates to determine the success or failure of treatment."**

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all my early grant applications, and I wasted far too much effort explaining that interventional oncology treatments are indeed useful in patients. I am hoping that interventional oncology has now become so critical for modern cancer care that these arguments are a vestige of the past.

**Q9** How have you acquired the leadership skills to establish and run your tumour ablation laboratory?

Leadership is all about finding the right people and letting them do their thing. If there's anything that I've done right in my time at Wisconsin, it's having the good fortune to work with great people who have carried our ideas forward.

**Q10** What are some points of emphasis that you incorporate into practice to be the best interventional radiologist you can be?

One thing that I think is under-appreciated in the procedural specialties is the impact of a great team and environment around you. Too often, the physician tries to play too many roles when performing a complex procedure. In my opinion, the physician who is delivering the needle or catheter should be thinking only about getting the device into the right spot and not about sedation, monitoring the patient, running a machine, adjusting imaging etc. We have purposely set up our ablation service to reflect this strategy,

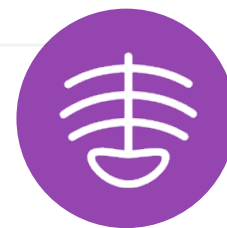
and we have an entire anaesthesia team to perform jet ventilation, as well as nurses and technologists to position the patient and run the CT and ultrasound machines. Each person is highly experienced in their role, which allows the physician to concentrate on delivering the device to where it needs to go.

One other point of emphasis that we have incorporated into our practice is to track every important outcome of every procedure that we do, no matter how minor. We know our complication and failure rates in near real-time, and we can adjust on the fly if something systemic appears to be going wrong. Without tracking your procedural metrics, it's very hard to improve.

**Q11** Are there any innovations on the horizon, specifically in the field of radiology and cancer imaging and therapy, that you think are particularly noteworthy?

I'm particularly interested in the impact of robotics combined with artificial intelligence and machine learning on image-guided procedures. I believe that advances in these areas in the next decade will revolutionise how we do even the most mundane procedures. Along with making image-guided procedures less invasive and more effective, we need to automate, standardise, and measure what we do if we are going to improve our outcomes across populations. ●

# Value-Based Radiology: A New Focus to Optimise Impact



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## VALUE-BASED RADIOLOGY: WHAT AND WHY?

Doctors have always liked to believe that what they do benefits their patients. It is, after all, intrinsic to our mission to "first, do no harm." Over the centuries, however, doctors have not always achieved this goal. Cupping and trepanning, for example, have not stood the test of time. Actually, attempting to measure the specific value to patients and to society of our interventions is a relatively recent development. Certainly, applying scientific principles to evaluating the safety and efficacy of medical interventions has been the standard for quite some time; however, going beyond diagnostic or therapeutic efficacy to consider the value created is quite a recent approach in medicine, and one that is still in development.

The concept of measuring value in healthcare, and moving towards a system whereby resources are dependent on value creation, owes much to the work of Michael Porter and his colleagues at the Harvard Business School, Boston, Massachusetts, USA, over the past 20 years, exemplified in his review paper on the

topic in 2010.<sup>1</sup> The fundamental idea involves moving away from resourcing being based on the volume of care delivered to one where it reflects the value delivered to patients and society.

Value as a concept in medicine can be difficult to define. Broadly speaking, to quote Warren Buffett: "Price is what you pay, value is what you get."<sup>2</sup> Much of the recent impetus behind the growing value-based healthcare movement is driven by the inexorable rise in the cost of healthcare in many countries, well in excess of the cost-of-living inflation. Between 1970 and 2020, healthcare expenditure in the USA rose from 6% of gross domestic product to 18%. In many other high-income countries, the increase in the same period has been 5 to 11%.<sup>3</sup> This trend is not sustainable; therefore, doctors must find some way of increasing the value of the care delivered without incurring additional costs and of making expenditure go further by ensuring it contributes positively to patient outcomes and society.

This applies to radiology as much as, or more than, other specialties. The increase in radiology utilisation in recent decades has been rapid.<sup>4</sup> Much of this is due to the constantly expanding



ability of radiology to identify and define illness, but not all of this increase contributes usefully to outcomes. A particular difficulty for radiologists in attempting to ensure the value of what is done is that much of a radiologist's work is influenced by factors beyond our control. Radiologists respond to referrers' requests and often lack the knowledge of patients' particular circumstances required to provide the freedom to decline requests or to suggest alternatives. Therefore, value-based radiology (VBR) must not only define and measure the value of a radiologist's work but must also influence referrals to optimise value.

So, let us consider what constitutes value in healthcare, including in radiology. It is about much more than reducing the costs of service delivery. In 2019, the European Commission defined value-based healthcare as being supported by four pillars:<sup>5</sup>

- Personal value: appropriate care to achieve patients' personal goals
- Technical value: achievement of best possible outcomes with available resources
- Allocative value: equitable distribution of resources across all patient groups
- Societal value: contribution of healthcare to social participation and connectedness

As doctors move from what helps an individual patient (personal value) to what benefits society as a whole (societal value), the value derived from healthcare is delivered to greater numbers of people. Thus, if doctors can identify healthcare interventions that can contribute societal as well as personal value (this may include restoring an individual to health so that they can continue to contribute to their family and society), doctors can enhance value delivery.

## VALUE-BASED RADIOLOGY: HOW?

How could these principles be applied to radiology? The European Society of Radiology (ESR) has been very active in VBR, publishing a concept paper on the topic in 2017<sup>6</sup> to introduce VBR to members and to initiate the consideration of how doctors can influence a pivot from

volume to value. Radiologists cannot expect that they can define what constitutes value to their patients; therefore, in 2019, the ESR surveyed patients across 22 countries to ask what aspects of radiology service delivery were of value to them.<sup>7</sup> The most common answers contained the expected responses (i.e., that there be no errors in diagnoses, the appropriate study be performed, diagnoses be delivered quickly, etc.); however, prominent among the feedback were items that might not have come immediately to radiologists' minds, such as that radiologists should be available to discuss imaging findings directly with patients.

Radiologists may believe that we deliver value by reporting imaging studies accurately and promptly, and we do, but patients are often unaware of that valuable contribution if they have no direct interaction with radiologists. Patients perceive the capacity to discuss a radiologist's findings as being an additional component contributing value beyond the radiologist's identification of those findings. Direct discussions about radiology findings between radiologists and patients will neither be required nor feasible in most circumstances; time, opportunities, and resources will often be lacking. Therefore, radiologists should not seek to impose ourselves into the middle of clinical relationships that already exist between referrers and patients. Conversely, there will be circumstances where taking the opportunity to engage directly with patients, ideally in conjunction with the referrer, will facilitate better understanding of the meaning of imaging findings, and, as a secondary gain to the specialty, enhance patient awareness of the contributions of radiologists. Patient representatives are increasingly seeking this possibility;<sup>7</sup> radiologists must try to meet that desire.

In 2019–2020, the ESR initiated and led a multisociety project with major radiology societies from North America, Australia, and New Zealand (American College of Radiology [ACR], Radiological Society of North America [RSNA], Canadian Association of Radiologists [CAR], Royal Australian and New Zealand College of Radiologists [RANZCR], and International Society for Strategic Studies in Radiology [IS3R]) to elaborate a joint multisociety statement on VBR.<sup>8</sup> This considered the many ways in which

radiology creates and delivers value to patients, and proposed practical actions that radiologists can take as a specialty to enhance value delivery. Delivering value in radiology is greatly dependent on co-operation with the referring doctors. With that in mind, the societies also jointly wrote a viewpoint article in a major medical (non-radiology) journal,<sup>9</sup> in an effort to initiate discussion with referrers and begin the process of joint work to enhance value.

In 2021, the ESR considered those activities in which we were already engaged in and that contribute value, and also what measures we could take in the near future to expand radiology's value contribution.<sup>10</sup> Most recently, the IS3R convened retreats involving radiology, industry, and patient representatives to define strategies to influence behaviours of patients, referrers, and radiologists in order to increase value and facilitate measurement of value created. This work is ongoing.

## VALUE-BASED RADIOLOGY: WHERE?

The value delivered by radiology to individual patients and to society encompasses both those aspects of a radiologist's work that are considered the traditional role, such as disease detection and diagnosis, and also broader and less immediately obvious contributions. Radiologists have a role in disease prevention by providing population screening for some conditions and by ensuring radiation protection standards are met. Radiologists must also include the reassurance provided to many patients and referrers by imaging that does not identify serious disease; while there are many reasons not to use imaging to exclude disease in patients without specific clinical indications, providing reassurance can be therapeutic and can enhance lives.<sup>8,9</sup>

Another important value contribution by radiology relates to monitoring the effectiveness of treatment and prognostication. By using imaging to differentiate responders from non-responders to specific treatments for many diseases, therapeutic pathways can be adapted to individual patients and outcomes can be positively influenced. Imaging can contribute to early identification of those patients who fail to

respond, allowing enhancement of life quality by ceasing treatments associated with morbidity and refocusing on good palliation.<sup>8,9</sup>

Communication represents an underappreciated component of value delivery in radiology. In many respects, much of the work of a diagnostic radiologist involves the sifting of imaging data to derive useful information, and then communicating that information to others in a manner that influences management. Given the constant pressure of work created by ever-increasing imaging volumes, it is all too easy to lose sight of this need for effective communication and to believe that a radiologist's job is done when we have reported findings of a study. Paying attention to the content, style, standards, and clinical relevance of the reports that are generated<sup>10-12</sup> to ensure the full importance of those reports is clearly understood by the referrer and using technological tools effectively to communicate unexpected, urgent, or critical findings can add value beyond report generation itself. Using multidisciplinary team participation to ensure that radiologic findings and options are fully considered in decision-making is one of the most important value creators available to radiologists. Taking all the opportunities to communicate directly with patients (which the ESR knows, from our survey, to be desired by patients)<sup>7,10</sup> can enhance value in helping patients to understand the role and capabilities of radiology in their care, and the relevance of their findings. Implementing this will not be easy, but radiologists must advocate for the resources and opportunities to allow such communication to take place if radiologists wish patients to understand our role and contributions.

What practical actions can radiologists take to add value? We should promote integration of clinical decision support tools such as the ESR iGuide<sup>13</sup> into requesting pathways for radiology studies. Such support tools should include the option of not requesting imaging, where imaging is unlikely to contribute usefully or answer the question being asked. Building in such expert-moderated guidance can reduce inappropriate imaging and increase timely use of the right test at the right time. As part of this initiative, radiologists should engage as much as possible directly with referring doctors, discussing individual patients and circumstances, and

thereby guiding them to justified, effective use of available radiologic modalities and expertise. Radiologists must pay attention to the justification of exposure to ionising radiation; pressure of work can often make it easier to just do what has been asked for, but by always ensuring appropriateness of imaging, radiologists contribute value to each patient and the population as a whole. Increasing availability of low-dose CT techniques can inculcate a belief among referrers that radiation doses are no longer a significant concern. However, radiologists must maintain caution about all radiation exposure and educate referrers that any inappropriate exposure should be avoided, however low the dose.

Radiologists must provide data to demonstrate the positive impact of our work on individuals and society. This will involve adapting much of the research we do from the lower-impact tiers of demonstrating technical or diagnostic efficacy of a particular technique or study to higher-impact measures, showing its impact on patient and societal outcomes.<sup>8,14</sup> This will not be easy; identifying the specific impact of radiology within a multispecialty programme of care for a patient is challenging.<sup>8</sup> Nonetheless, radiologists can and must design research studies to achieve this if we want to have their contribution recognised.

Restricted investment in radiology can produce bottlenecks, reducing overall system efficiency;<sup>8</sup> for example, requesting cross-sectional imaging for a patient attending an emergency department increases their average length of stay.<sup>15</sup> If hospital-based imaging facilities are insufficiently resourced to deal with demands rapidly, the efficiency of expensive hospital-based care is compromised. Furthermore, a failure to resource imaging services to provide appropriate access to primary care or outpatient referrers results in increased reliance on more expensive hospital-based care.<sup>8</sup> Radiologists must act as advocates to managers and funders of healthcare to ensure adequate resourcing of our services to meet justified demand. Reductive views of the role of radiologists as being solely producers of reports on imaging studies are common. Radiologists must be vocal in explaining to those who make resourcing decisions that their role, and the

value we contribute, encompasses much broader inputs into healthcare, and that the maximum value of radiology can only be realised by providing sufficient resources to fulfil their role in as complete a manner as possible.<sup>16</sup>

Within radiology departments, radiologists must ensure that resources are utilised for maximum benefit. If patients need access to 24 hours a day, 7 days a week emergency care, radiologists must configure our services to provide that (and must be resourced to do so). Radiologists must avoid temptations to isolate resources for the benefit of particular subspecialties or groups of patients if those same resources can be used more efficiently for every patient; siloed budgets and subdepartments may not be the best use of expensive equipment and staff.<sup>8</sup> Radiologists must always be open to considering what we could change to increase value. Key to this is maintaining a constant culture of quality improvement, auditing diverse aspects of services, and adapting them where this would help us increase standards.<sup>17</sup> Radiologists must take every opportunity to play an important role in multidisciplinary team decision-making as an intrinsic part of our work rather than an unwelcome intrusion on reporting activity.<sup>16</sup>

## VALUE-BASED RADIOLOGY: WHO?

Ultimately, creation and enhancement of value in radiology is a joint responsibility of all concerned. Radiologists can do much to enhance value (some suggestions are given above) and must stay aware of evolving concepts of value and the metrics used to assess it. Referrers must engage with radiologists to ensure that their requests for radiology services are supported by evidence, justified, and optimised to the particular circumstances of a given case. Patients must be educated and supported to understand that more elaborate, more expensive, or simply more imaging may not always be the best application of resources to their particular clinical need at any given moment in time. All involved parties must appreciate that resources are finite, utilisation must be matched to availability, and critical evaluation of value must be part of every application of radiology to patient care.<sup>8,9</sup>



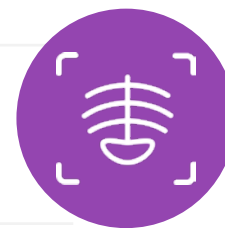
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# Ultrasound in Polycystic Ovarian Syndrome: What? When? How? Why? Who?

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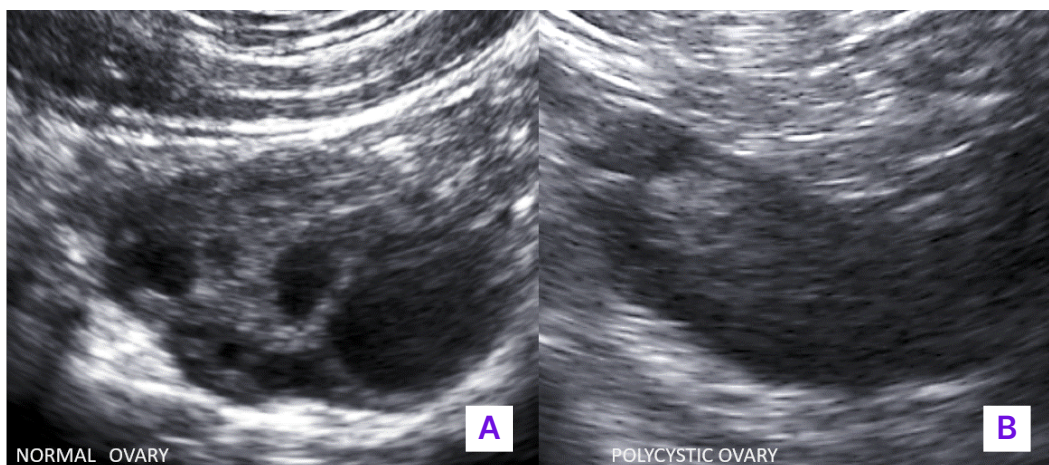
## INTRODUCTION

Assessment of ovarian morphology is one of the most commonly performed ultrasound examinations. Polycystic ovarian syndrome (PCOS) is a multi-factorial, multi-faceted, polygenic disorder with varying phenotypes. It defines labyrinthine symptomatology including menstrual cycle irregularities, hormonal imbalance, and metabolic disturbance. Historically, this syndrome has been diagnosed clinically with supportive lab parameters. However, the role of ultrasound has mutated from identifying, to misdefining, and finally to reclassifying PCOS.<sup>1-4</sup> At present, it seems that the ultrasound identification of the 'string of pearls' has cemented this disease with a misleading name. A seeming increase in the detection of polycystic ovarian morphology on ultrasound has been accredited to advances in technology allowing better visualisation of the ovaries, or stroma, or follicles by higher frequency probes with the possibility of endovaginal imaging. Nevertheless, there is a disparity in what the ultrasound shows, how the clinician interprets the report, and what the patient understands about their diagnosis. Identification of the multi-follicular ovary is still quite frequently ascribed to PCOS, while ovarian ultrasound remains ambiguous to the different

phenotype of PCOS. Whether morphological disparities represent a normal variation in ovarian anatomy or true precursors of PCOS remains debatable. The absence of a definition of a 'normal' ovary, with respect to volume and follicular number, makes the diagnosis of PCOS more challenging.<sup>5,6</sup>

Over time, ovarian volume remains the most reliable, reproducible, and sensitive method for the identification of PCOS (Figure 1). However, it has a lower diagnostic accuracy due to considerable overlap with normal females. Confusion prevails in the setting of pelvic infection, hormonal treatment, and ethnic variability. In the setting of poor image resolution, whether due to the use of lower frequency probes or patient habitus, volume remains the best usable criterion.<sup>3,6</sup> While endorsing the Rotterdam criteria, the recent 2018 International Evidence-Based Guidelines also acknowledged the fact that ultrasound criteria are evolving and new thresholds need to be established. This development is accredited to both accelerated development in technology as well as increased availability of ultrasound in widespread populations. However, it should be mentioned that technical skill varies widely, and as such it is important to realise that it is not only the development of 'defined criteria' but

Figure 1: A) Normal versus B) polycystic ovaries (B mode, transvaginal).



The normal ovary is smaller in size, has few randomly distributed follicles of varying sizes interspersed within the stroma. In contrast in a typical polycystic ovary, both the length and width are increased as well as the ovarian area. The follicle number, with a diameter mainly between 2 and 5 mm, is more than 12. The distribution within the ovaries is mainly peripheral. The increased and hyperechoic stroma occupies the centre of the ovaries.

Figure 2: A multifollicular ovary (B mode, transvaginal). It shows multiple antral follicles predominantly 4–10 mm in size, more so in a random distribution without pre-dominance of stroma.

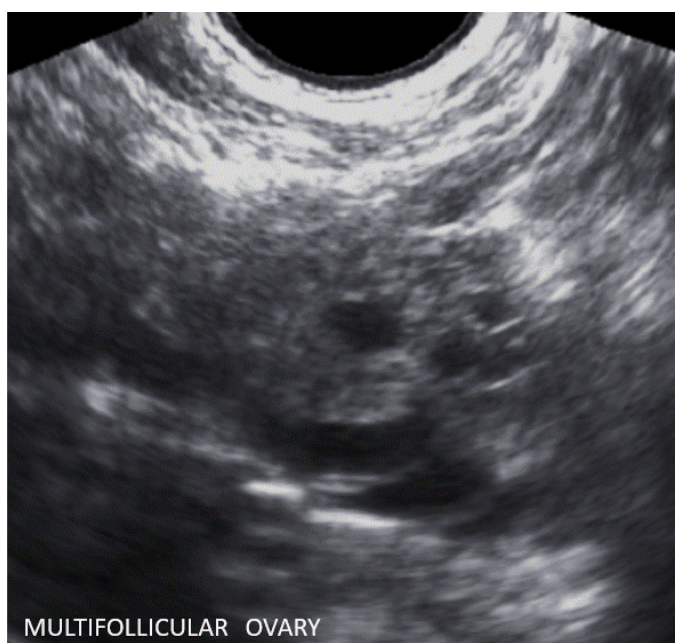
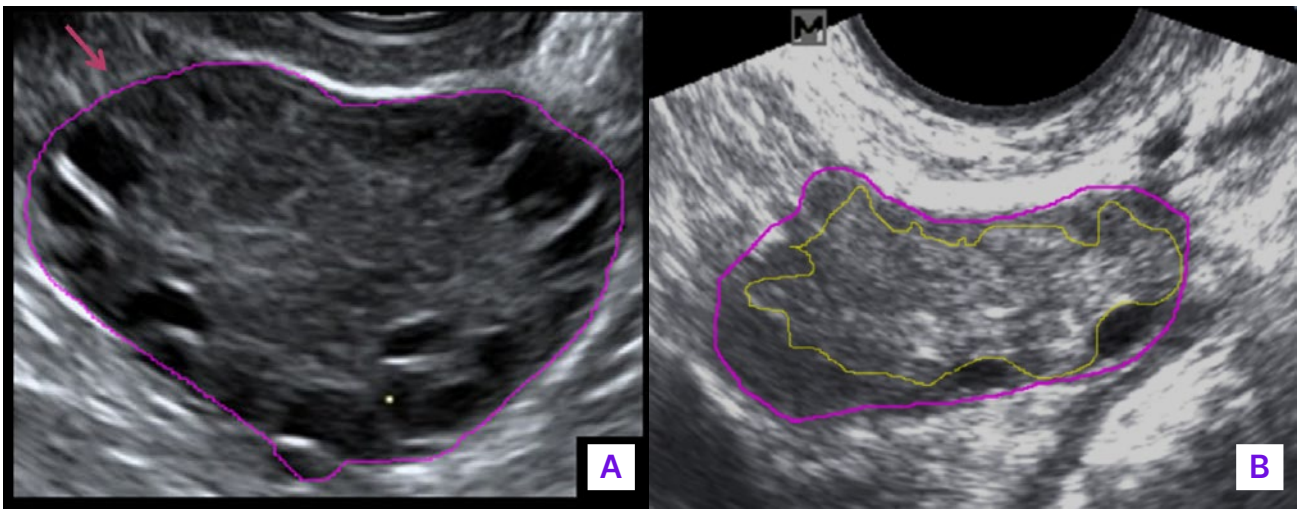




Figure 3: Measurement of ovarian/stroma ratio (B mode, transvaginal).



**A)** Ovarian area was measured by outlining the external limits of the ovary with an electronic caliper tool (pink). **B)** Stromal area was measured by outlining the peripheral profile of the stroma, avoiding antral follicles represented by anechoic structures in the ovary (yellow). The outline was extended to the periphery of the ovary when no follicles were present around that peripheral portion of the ovary.

also the distribution of skill and expertise among practitioners, which will determine the diagnosis of PCOS at a community level.<sup>4</sup>

Assessment of the number of follicles has been upheld to be one of the specific features of PCOS. The concept is to sweep through the entire ovarian volume and count the number of follicles in each ovary in totality, keeping in mind not to measure sonolucencies (<2 mm) as they do not represent actual follicles (Figure 2). Grid systems, tagging, and marking have been used in post-processing to accurately measure the follicular number per ovary (FNPO) in order to improve reliability and reproducibility. However, these methods are time-consuming and not widespread. Though there have been documented ethnic variations, generally patients with PCOS are seen to have a higher number of follicles per ovary. The FNPO has been found to be the best-describing feature in cases of unilateral PCOS. The distribution of follicles has also been proposed to help identify 'classic PCOS', though its accuracy remains in doubt. Disordered follicular growth and recruitment have been identified using ultrasound as well. Transvaginal ultrasound allows a superior assessment of follicles than transabdominal ultrasound, and should be utilised whenever

possible. However, in circumstances involving cultural or personal barriers, transabdominal remains the only modality widely accepted.<sup>3,4,6-11</sup>

Bright, echogenic stroma has been subjectively accredited to PCOS. There have been many efforts to correlate qualitative indexes of stromal echogenicity with PCOS; however, it has been found that the intrinsic echogenicity of the ovarian stroma is no different in PCOS than in the normal ovary. 'Feature analysis' objectively measures the brightness, or echogenicity, of the ovarian stroma. This is done by measuring the intensity level of the ultrasound pixels within the stroma displayed on an ultrasonic image. The mean echogenicity of a given area can then be calculated. A study by Buckett et al.<sup>12</sup> found that even though the stromal index was significantly elevated in polycystic ovaries, the mean stromal echogenicity was not different. The subjective 'bright' stromal echotexture in polycystic ovaries is attributed to a synergistic effect of an increase in ovarian stromal volume, and hence a relatively lower mean echogenicity of the entire ovary.<sup>6,12</sup> The stromal or total ratio has also been found to have high sensitivity and specificity, albeit with poor reproducibility (Figure 3). With the improvement in ultrasound software, the brightness or echogenicity of the ovarian stroma

can be determined much more objectively, and therefore, the quantification of ovarian stroma, by computerised reading of ultrasound images, has revealed that stromal hypertrophy is a frequent and specific feature in ovarian androgenic dysfunction, with some studies demonstrating that increased stromal volume correlates positively with serum androgen level.<sup>6,14</sup> However, no standardised method exists for determining stromal volume. Because overall ovarian volume correlates well with stromal volume in polycystic ovaries and is more easily measured in clinical practice, the determination of overall ovarian volume is a reliable surrogate for ovarian stromal assessment.<sup>6,13,15</sup>

Elevation of impedance indices of the uterine arteries has been described in patients with PCOS, though it seems a multitude of factors contribute to this finding, including the coexistence of obesity. A higher pulsatility index and systolic or diastolic ratio has also been described. Since most of these studies are performed on patients primarily concerned with infertility, it is not known where exactly these findings fit in the pathophysiology of PCOS.<sup>1,16-19</sup>

The 3D ultrasonography allows accurate measurement of the stromal volume, follicular number, and ovarian volume. Accuracy is comparable to 2D ultrasound with ample agreement of the Rotterdam criteria. Although promising, 3D ultrasound is relatively expensive and not widely available.<sup>20,21</sup>

The imaging of ovaries on magnetic resonance is a new and exciting frontier. Ovarian volume on MRI has been shown to be quite sensitive for diagnosis, with high reproducibility. Peripheral follicular distribution and FNPO >28 are supportive, but not as reproducible. Although there are advantages of MRI in patients diagnosed with obesity, poor quality scans are obvious; MRI can't be extrapolated to the entire 'PCOS eligible' population due to sheer number and cost.<sup>6,22</sup> Artificial intelligence and convolutional neural networks form another exciting area which, however, may not translate to clinical practice soon, or be enough.<sup>23</sup>

## WHAT?

A specific protocol, as laid down by the 2018 International Guidelines, is quintessential to the proper evaluation of PCOS. This protocol should not be limited to this syndrome but extended to all gynaecological ultrasound evaluations.<sup>4</sup>

## WHEN?

The ultrasound scan preferably should be performed the scan on Day 2–7 of the menstrual cycle. This prevents any growing follicle from hiding smaller ones or modifying ovarian volume. In case of females with Oligo or amenorrhoea, scanning may be performed at random or 2–5 days after progesterone induced bleeding.<sup>4</sup>

## HOW?

Scanning should be done with an 'optimally' filled bladder, avoiding extremes in transabdominal sonography (TAS), and an empty bladder in transvaginal sonography. Identify the ovaries in relation to iliac vessels. The entire ovary should be scanned in two orthogonal planes. Measurement of ovarian volume (length X width X thickness) should be done precisely with ensuring adequate visualisation of the ovarian contour. If possible, a follicular count should be obtained with a careful meticulous sweeping of both ovaries individually. This count may not help in the diagnosis of a particular patient, but will help long-term to allow healthcare professionals to redefine criteria. If the setting allows, estimation of the stromal area should be done offline. Additionally, an assessment of the liver and pancreatic fat grade should be included, as well as the adrenal areas.<sup>4</sup>

## WHY?

One of the guidelines that stood for the author, but is rather ignored in daily practice, is the 'non-inclusion of ultrasound in the diagnosis of PCOS in adolescents with gynaecological age of less than 8 years.' So why include an ultrasound in this age group? It is not just PCOS that can cause pathology in this population. The author emphasised having to think beyond PCOS as well. The role of ultrasound varies with

the patient's age and primary concern, from dermatological troubles to fertility treatment, and it needs to be tailored accordingly.<sup>4</sup>

## WHO?

A common core protocol should be followed by every person performing the ultrasound. Reporting needs to be standardised and uniform. Establishment of ethnic thresholds should be considered. It should be understood that the criteria for TAS and transvaginal sonography are not the same. The prioritisation of the volume

criteria in TAS and low resolution and/or difficult scans is also to be acknowledged.<sup>4</sup>

The sheer number of patients requiring an ultrasound for evaluation of ovaries implores the establishment of reliable, easy-to-follow, reproducible, and accurate ultrasound protocol. Radiologists, as well as sonographers, should undergo sensitisation so as to make the reporting of ovarian ultrasound uniform. Perhaps a large-scale normal ovarian morphology nomogram preparation is the need of the hour, with emphasis on differences in ethnic origin. Finally, it should be remembered that ultrasound is only a brushstroke in the masterpiece that is PCOS.

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# Imaging of Ovarian Cancer: From Early Detection to Post-treatment Relapse

## Editor's Pick

Our Editor's Pick featured article focuses on ovarian cancer, where successful treatment often depends on early detection. In this review, Forstner provides a practical update on the role of imaging throughout every phase of the ovarian cancer disease course. This includes an analysis of the utilisation of sonography for cancer detection and characterisation, MRI as a complementary tool for indeterminate findings, and CT for ovarian cancer staging. The benefits of CT are also discussed in relation to selecting patients suitable for medical therapy and providing pivotal information for individualised treatment.



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## Abstract

Ovarian cancer refers to a multitude of different cancer types originating from or involving the ovaries. Although it ranks third in gynaecological cancers, it is among the deadliest cancers in females. The prognosis mainly depends on early detection, but the majority of cases are diagnosed at advanced stages. Exact tumour delineation is crucial for individualised therapy planning. This review will provide a practical update of the role of imaging in every phase throughout the course of this disease. The imaging technique of choice depends mainly on the clinical setting. Sonography remains the first-line imaging modality for cancer detection and is the most important for characterisation of adnexal masses. MRI is a valuable complementary imaging tool in sonographically indeterminate findings. For ovarian cancer staging, CT is considered an optimal imaging technique. CT renders all critical information for treatment stratification. It assists in surgery planning by displaying the load and the distribution of the disease and alerts to sites difficult to resect. It also renders critical information in selecting patients more suitable for medical therapy. In a females treated for ovarian cancer, imaging is only recommended when there is suspicion of recurrence, where CT and PET/CT are most commonly used to confirm relapse and provide pivotal information for individualised treatment.



## Key Points

1. Ovarian cancer is among the most harmful cancers in females and is generally diagnosed at a late stage, when the prognosis is poor. Moreover, despite optimal therapy, the relapse rate of ovarian cancer is as high as 70–85%. Almost 25% of females will relapse within 6 months and in most cases the cancer will recur within 2 years after completion of therapy.
2. Imaging plays a pivotal role throughout the course of the disease: from the characterisation of adnexal masses to treatment planning, and confirmation of suspected ovarian cancer relapse.
3. Imaging gives crucial information for selecting candidates eligible for cytoreductive surgery. In this case, PET/CT is useful to demonstrate small or distant metastases. It is also optimally combined with MRI as it provides the single best modality for local surgery planning.

## INTRODUCTION

Currently, ovarian cancer is recognised not as a single entity but as an umbrella term that refers to different malignancies arising from or involving the ovaries.<sup>1</sup> The vast majority (85–90%) of ovarian cancers constitute of epithelial ovarian cancers (EOC) that mostly affect females who are peri- and post-menopausal age. Recent advances in molecular and genetic analysis distinguish between five major histopathological subtypes of EOC, which differ not only in terms of origin, precursor lesions, prognosis, and molecular characteristics but also in emerging therapeutic implications.<sup>2,3</sup>

In fact, it is well established that premalignant precursors of high-grade EOCs, the most common type of ovarian cancer, and *BRCA*-associated cancers are arising not in the ovaries but in the distal fallopian tube.<sup>1</sup>

Although in the past four decades there has been an improvement in the 10-year survival rates from 18–35%, ovarian cancer is still among the deadliest cancers in females.<sup>4</sup> This is mostly due to the fact that ovarian cancer is diagnosed at an advanced stage, when prognosis is poor, and, despite optimal initial treatment, it takes a fatal course characterised by serial relapses. Conversely, detection of ovarian cancer at an early stage or, ideally, of precursor lesions is associated with an excellent prognosis.

Imaging plays a pivotal role in females with ovarian cancer throughout the course of their

disease: for the characterisation of adnexal masses, treatment planning of ovarian cancer, and confirmation of suspected ovarian cancer relapse. From the beginning, disease imaging renders pivotal information for individualised tailored treatment.<sup>5</sup> The selection of the appropriate imaging technique depends on various factors, but mostly on the clinical scenario. This review will focus on the value of the different imaging modalities used in assessing ovarian cancer.

## EARLY DETECTION OF OVARIAN CANCER

### Screening

Due to the lack of or only vague clinical symptoms, the vast majority of ovarian cancer is diagnosed at a late stage, when the prognosis is poor. The clinical impact of diagnosing invasive ovarian cancer or precursors such as borderline tumours early would be enormous.<sup>6</sup> Early detection is the only way to achieve a high survival rate in females with ovarian cancer. Stage I ovarian cancer has an excellent 5-year survival rate of more than 90%.<sup>7</sup> A recent comprehensive analysis of subtypes extracted from 28,118 ovarian cancers of the Surveillance, Epidemiology, and End Results (SEER) Program database showed that 39.2% of EOCs are diagnosed in Stages I and II. Of note, these tend to present the more indolent Type I ovarian cancers. In contrast, Type II (high-grade cancers and carcinosarcomas) tumours accounted for the vast majority of advanced stage cancers

and were associated with a poor outcome independent of the stage.<sup>8</sup>

Unfortunately, there are no existing, effective strategies for screening ovarian cancer using imaging, rapidly emerging biomarkers, or a combination.<sup>9</sup> At present, screening for females with a normal-risk of ovarian cancer is not recommended.<sup>9</sup> Data from large screening programmes failed to show a survival benefit of females who were screened compared with females who were not screened.<sup>10,11</sup> The rate of detected ovarian cancers was low, the performance in detecting Stage I disease was limited, and harms related to false positive testing were seen.

However, in females who are at high-risk of ovarian cancers due to *BRCA* mutations, a family history of ovarian cancer, or Lynch syndrome, semi-annual screening is recommended. Such a predisposition is estimated to occur in 10–15% of ovarian cancers. Carriers of the *BRCA* mutation have an increased life-time risk of ovarian cancer. It is estimated that carriers of the *BRCA1* and *BRCA2* mutations have an increased life-risk of 40–45% and 15–20%, respectively, by age 70.<sup>6,9</sup> These females also tend to develop ovarian cancer in younger ages, but ovarian cancer is rarely found under the age of 40.<sup>9</sup> In this population, transvaginal ultrasonography is generally accepted as the optimal imaging test for screening for ovarian cancer. Due to its high specificity, MRI can be offered for further characterisation of sonographically indeterminate masses. Thus, it may assist in reducing the number of surgical interventions if physiological ovarian masses or uterine fibroids are detected.<sup>12</sup> Current evidence supports that prophylactic salpingo-oophorectomy reduces the ovarian cancer risk. It is recommended in the high-risk population, aged 35–40, or after the completion of childbearing.<sup>9</sup>

### Prediction of Malignancy in Adnexal Masses

The accurate characterisation of an adnexal mass is essential for appropriate patient management.<sup>13</sup> Likely benign lesions can be managed conservatively or by laparoscopic surgery, whereas females with malignant lesions will benefit from treatment by gynaecological oncologists or in cancer centres.<sup>12,14</sup>

Advanced ovarian cancer usually requires radical cytoreductive surgery, followed by chemotherapy, or, alternatively, neoadjuvant chemotherapy, followed by interval debulking.<sup>15,16</sup>

Several imaging-based models for preoperatively assessing the risk of malignancy of an adnexal mass have been developed. These include the pattern recognition approach, e.g., the commonly used International Ovarian Tumour Analysis (IOTA) simple ultrasound (US) rules or other mathematical models developed by the IOTA, Risk of Malignancy Index (RMI), the Gynaecologic Imaging Report and Data System (GI-RADS), and the recently published Ovarian-Adnexal Reporting and Data System (O-RADS) risk stratification system.

Transvaginal sonography, combined with Doppler techniques, remains the mainstay for assessing adnexal masses. Due to its clinical utility and cost effectiveness, it has been established as the first-line imaging modality.<sup>17</sup> It performs excellently in evaluating cystic adnexal lesions, which constitute the vast majority of adnexal masses. However, MRI is generally considered as a second-line, problem-solving modality and is particularly useful in complex or solid adnexal masses and when the clinical likelihood of malignancy is low.<sup>12</sup> A systematic review demonstrated that the major advent of MRI is its high specificity to provide a confident diagnosis of benign adnexal lesions.<sup>18</sup>

Pattern recognition analysis, the gold standard for analysing an adnexal mass, is highly dependent on the level of expertise. Transvaginal sonography yields sensitivities of 85% and specificities of 90%, which might be even higher if they were performed in expert centres.<sup>19,20</sup> The value of grey scale and colour Doppler US has been extensively analysed by the IOTA. Subjective assessment by highly trained clinicians in US performed equivalently to mathematical models such as the IOTA-simple rules models and logistic regression models.<sup>21</sup> The combination of imaging techniques, usually with US, clinical features, and cancer antigen-125 (CA-125) levels is the basis of scoring in the RMI.

Recently, the O-RADS scoring and management system was introduced.<sup>13,22</sup> This 5-point risk classification system for ovarian or adnexal masses was developed in close co-operation

for US and MRI by the American College of Radiology (ACR) O-RADS Committee. A standardised imaging technique and terminology should be used for risk categorisation at initial diagnosis, as well as for the follow-up. In the US O-RADS score, ovarian masses are categorised based on their morphology and Doppler assessment. Incomplete evaluation (Score 0) and physiological ovarian follicles (score 1) are separated from almost certainly benign (Score 2: <1%) masses, low risk of malignancy (Score 3: 1–<10%), intermediate risk (Score 4: 10–<50%), and high risk (Score 5: >50%) masses.<sup>22</sup>

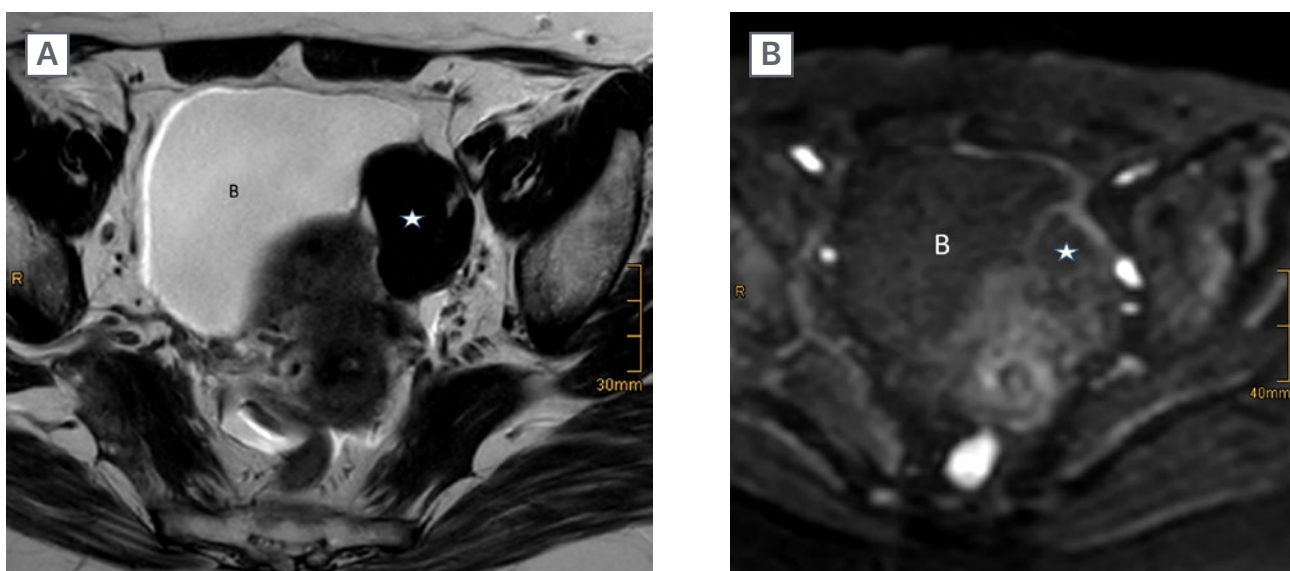
US and MRI O-RADS were implemented to provide a standardised risk stratification system for ovarian and adnexal masses, which should serve as a consistent basis for analysis and reporting.<sup>13,22</sup> O-RADS scoring should only be used in average-risk patients with no acute symptoms. It is also aimed at providing a guidance for management of adnexal masses in clinical practice. The integration of the risk score in the reports is ultimately intended to improve communication with referring clinicians by eliminating uncertainties in term usage and to assist in clinical decision making.<sup>13</sup>

However, clinical management directed by the treating physician supersedes management recommendations, based on imaging alone.<sup>13</sup>

Even in the hands of experts, 5–22% of adnexal masses will remain sonographically indeterminate or difficult to classify.<sup>23</sup> Such masses typically exhibit the following sonographic features: large size, uni- or multi-locular, with solid aspects, irregular walls, papillary projections, and multilocular cysts. The vast majority of these lesions are benign tumours at histopathology, mostly cystadenomas, cystadenofibromas, and fibromas.<sup>23–25</sup>

To date, MRI is usually performed as a complementary imaging tool to further characterise adnexal masses that are indeterminate on US (Figure 1).<sup>12</sup> The European Society of Urogenital Radiology (ESUR) guidelines recommend an algorithmic approach using basic and problem-solving sequences that will allow a confident diagnosis in the majority of cases, and thus assist in stratifying patients to the most appropriate treatment.<sup>12</sup> Thomassin et al. introduced a 5-point risk score that combined morphologic pattern analysis, diffusion-weighted

**Figure 1: Left ovarian thecoma in a 55-year-old-female.**



Sonography showed an indeterminate solid mass. A solid tumour (asterisk) is shown as separate from the uterus and adjacent to the bladder (B). MRI showed typical features of a benign tumour with low signal intensity on T2WI (A) and DWI (B) using a high b-value.

DWI diffusion-weighted imaging; T2WI: T2 weighted image.

**Table 1: Magnetic resonance Ovarian-Adnexal Reporting and Data System™ Scoring classification system\*.**

O-RADS MRI score	Risk category	PPV for malignancy (%)
0	Incomplete evaluation	N/A
1	Normal ovaries	N/A
2	Almost certainly benign	<0.5
3	Low risk	Approx. 5
4	Intermediate risk	Approx. 50
5	High Risk	Approx. 90

The PPV values for malignancy include both borderline tumours and invasive cancers.

\*Adapted from Reinhold C et al.<sup>13</sup>

†Approximate PPV based on data from Thomassin-Naggara I et al.<sup>27</sup>

Approx: approximately; PPV: positive predictive value; O-RADS: Ovarian-Adnexal Reporting and Data System.

imaging, and perfusion analysis of solid tissue within an adnexal mass using time intensity curves.<sup>26,27</sup> Recently, this MRI O-RADS score has been validated in a large European multicentre study. The results demonstrate a robust score, with sensitivities of 93% and specificities of 91%, for detecting malignant lesions in sonographically indeterminate masses, regardless of the level of radiological expertise.<sup>6,27</sup> Data from this study also provided the evidence for the MRI O-RADS risk stratification scoring system (Table 1).

## IMAGING FOR TREATMENT PLANNING IN OVARIAN CANCER

Traditionally, newly diagnosed ovarian cancer is surgically staged according to the International Federation of Gynaecology and Obstetrics (FIGO) or Tumour, Nodes, Metastases (TNM) staging classification. The 2014 updated FIGO system provides not only tumour stage categorisation but also incorporates information of the histological subtype and grade.<sup>28</sup>

Staging is usually performed during a staging laparotomy, including upfront cytoreductive surgery and is followed in most cases by taxane- and platinum based chemotherapy.<sup>16</sup> It has been

established that cytoreduction to a cut off of 1 cm (optimal cytoreduction) is associated with increased survival in ovarian cancer.<sup>29</sup> However, a trend towards ultraradical surgery, with complete resection of all gross tumour deposits, can be noted.<sup>30</sup> The reported rates of optimal cytoreduction vary broadly from 15–85%, with high-volume oncologic centres achieving rates of optimal cytoreduction of up to 60–75%.<sup>31,32</sup>

The optimal treatment for the advanced cancer Stages IIIC and IV has long been a subject of debate.<sup>16,30</sup> Recent data support that in advanced ovarian cancer, neoadjuvant chemotherapy renders equivalent survival outcomes but lacks the issue of high perioperative complications of ultraradical surgeries.<sup>16,30</sup>

CT has been established as an important tool not only for preoperative staging of ovarian cancer but also for providing pivotal information for management decisions.<sup>5</sup> It is the mainstay of ascertaining the extent of the disease and exact depiction of distribution of the metastatic dissemination. It may also alert to sites that might be difficult to completely resect and where a multidisciplinary approach during surgery may be appropriate.<sup>33</sup> Thus, it provides pivotal information for selecting between patients



Figure 2: CT of advanced ovarian cancer.



*Staging CT demonstrates a large solid and cystic pelvic mass (asterisk) adjacent to the uterus. Large amounts of ascites are seen, as well as peritoneal implants at the dome of the right diaphragm (arrow).*

suitable for upfront cytoreductive surgery and those more likely to benefit from medical therapy prior to surgery, e.g., due to extreme tumour load or in patients unfit for surgery.<sup>34</sup> When neoadjuvant chemotherapy is planned, an image-guided biopsy can be offered to confirm the diagnosis of disseminating ovarian cancer and to identify the histological subtype.<sup>33</sup>

Dissemination via the peritoneal cavity beyond the pelvis is typical for ovarian cancer and is found in more than 60% of females at diagnosis (Figure 2). The vast majority of these will present with high grade EOC. Solid or more diffuse peritoneal deposits are commonly found in the omentum, diaphragm, liver or spleen surface, the bowel, mesentery, and along peritoneal reflections. Perihepatic metastases (Stage III) present as a typical liver manifestation in newly diagnosed ovarian cancer. They usually present

scalloping lesions with smooth margins along the liver surface but may sometimes invade the liver surface.<sup>35</sup>

Structured reporting of CT in ovarian cancer is a powerful tool of providing crucial information for therapy decisions in multidisciplinary meetings. The ESUR guidelines suggest not only defining the stage according to the FIGO or TNM classification but strongly recommend a management-driven, structured report that includes comprehensive information of the primary tumour, including the tumour burden and sites of the metastatic disease, as well as other information relevant for treatment planning.<sup>33</sup> Potentially difficult to resect disease (not optimally resectable) should also be highlighted in the report. Although the clinical practice varies, these include tumour deposits of >2 cm in size in the root of the mesentery, gastrosplenic

ligament, lesser sac, porta hepatis and falciform ligament, and suprarenal or supradiaphragmatic lymphadenopathy.<sup>34</sup> Various tests have been developed to predict the likelihood of optimal cytoresection.<sup>31,32,36</sup> Major determinants include clinical risk factors, CA-125 levels, and imaging tests, most commonly using CT. However, the clinical utility of such standardised prediction of resectability could not be proven.<sup>24,31,32</sup>

To date, preoperative staging of ovarian cancer remains a CT domain. It is widely available, reproducible, and provides all relevant information for staging in a short examination time.<sup>33</sup> The reported accuracy for all stages ranges from 70–90%, with an overall sensitivity in detection of peritoneal implants of 85–93%.<sup>34,47</sup> Limitations, however, include small volume peritoneal disease (<5 mm) and sites such as the bowel surface and the mesentery. PET/CT is not routinely used for initial staging of ovarian cancer but may be useful as an adjunct test to inconclusive CT findings or in case of contraindications for contrast media.<sup>33,38</sup> Although MRI performs similarly for staging and is superior to CT in the visualisation of small peritoneal implants, it is still regarded as a second-line imaging modality.<sup>33,38</sup> Apart from costs, this is mainly attributed to technical issues and a much longer examination time. MRI is recommended when radiation exposure or its superior soft tissue contrast capability is an issue, e.g., in pregnancy or in young females presenting with presumed borderline tumours and if fertility preservation is considered.<sup>38</sup> Similarly, the role of fluorodeoxyglucose-PET/CT remains that of a problem solving imaging test, that is particularly useful in advanced ovarian cancer or as an alternative to contraindications of contrast-enhanced CT. Whole body MRI has shown excellent results and performs comparably to PET/CT for assessing metastatic disease within and outside the abdominal cavity.<sup>39</sup> As this imaging technique is emerging from research to clinical application, it may become a central management tool in newly diagnosed ovarian cancer.

## PREDICTION OF TUMOUR RESPONSE IN OVARIAN CANCER

Neoadjuvant chemotherapy prior to cytoreductive surgery is a treatment option

in selected patients with advanced EOC. Clinical, routine serial CA-125 assessments and CT serve as the mainstay for response assessment during this therapy. CT is usually performed as a baseline study and after 3 cycles of chemotherapy to determine eligibility for cytoreductive surgery. Alternatively, in insufficient response medical treatment is continued.

Assessment of the change in tumour load is a critical feature in patients undergoing clinical trials. Here, response has traditionally been assessed by serial CA-125 monitoring and standardised quantification of the tumour using Response Evaluation Criteria in Solid Tumours (RECIST), mostly in CT. In ovarian cancer, however, application of the RECIST criteria is challenging due to the diffuse peritoneal spread in most cases of EOC and the problem of defining target lesions.<sup>40</sup>

A recent, large multicentre study conducted in patients undergoing neoadjuvant chemotherapy showed that response criteria using only CA-125 or RECIST were limited to predict optimal cytoreduction.<sup>41</sup>

CA-125 is the currently best-established biomarker in ovarian cancer. However, a multitude of potential novel biomarkers are under investigation. Moving forward to individualised treatment of ovarian cancer, research activities include comprehensive molecular profiling of tissue biopsies and of tumour DNA circulating in the blood (liquid biopsies).

Prediction of tumour response prior to therapy is also an area of ongoing research, utilising the functional imaging techniques of PET/CT and MRI.<sup>40</sup> In one study, apparent diffusion coefficient quantification obtained by diffusion-weighted MRI showed differences between the primary tumour and peritoneal metastases, reflecting inter-site tumour heterogeneity and potentially resulting in different biological effects.<sup>42</sup>

Radiomics and radiogenomics data render information beyond the morphological tumour manifestations. Radiomic signature of the primary tumour and deposits based on preoperative CT may provide information as a prognostic imaging biomarker in high-grade

ovarian cancer.<sup>43</sup> The role of both intra- and inter-site heterogeneity in ovarian cancer has been addressed by Vargas et al., who showed that CT radiomic features of tumour heterogeneity were associated with a poorer outcome and incomplete surgical resection.<sup>44</sup> In the future, the combination of radiomic features and clinical data may allow for the development of predictive models of resectability or of tumour progression.<sup>45</sup>

## IMAGING OF THE TREATED OVARIAN CANCER

Despite optimal therapy, the relapse rate of ovarian cancer is as high as 70–85%.<sup>45</sup> Almost 25% of females will relapse within 6 months and, in the majority, the cancer will recur within 2 years after completion of therapy.<sup>46</sup> In advanced ovarian cancer, the 5-year overall survival rate differs across the different subtypes of EOC.<sup>47</sup>

When ovarian cancer has relapsed, it is a treatable but rarely curable disease. In general, relapse introduces a chronic and consecutively lethal stage of the disease, with reported survival rates ranging from 12–32 months.<sup>48</sup> Survival after the relapse is related to several factors including chemosensitivity, the time of progression-free interval after therapy, and the number of recurrent lesions. The standard of care for recurrent ovarian cancer is systemic platinum-based chemotherapy or subsequent line therapies. Secondary cytoreductive surgery is not routine but may be performed in selective patients.<sup>48</sup> This individualised approach depends on the size and site of the recurrent disease and is usually based upon a multidisciplinary conference decision.<sup>49</sup> Cytoreductive surgery for relapsed ovarian cancer is mostly performed in the localised disease at its first recurrence or after a long disease free-interval.<sup>49,50</sup> Patients with a prolonged platinum-free interval (>6 months) and those with an isolated or limited volume of disease and a positive Arbeitsgruppe Gynäkologische Onkologie (AGO) score are likely to benefit from secondary surgery compared with those with a shorter progression-free interval or large volume disease.<sup>50</sup>

Although there is lack of evidence that routine imaging after completion of primary therapy improves survival in ovarian cancer, in clinical practice CT is commonly used for surveillance in females in clinical remission.<sup>51</sup> Major gynaecological guidelines, however, advise against routine imaging in a patient treated for ovarian cancer.<sup>48,49,51</sup> Surveillance is recommended by clinical assessment and CA-125 monitoring for 3–4 months in the first 2 years and in a 6 months interval for Years 3–5. Imaging in a female treated for ovarian cancer is only recommended if recurrence is suspected, e.g., in rising CA-125 levels or in clinical symptoms suspicious of relapse.<sup>48</sup>

Ovarian cancer usually relapses in the abdomen or the pelvis, with recurrence found in the surgical bed in up to 50% of patients.<sup>52</sup> Peritoneal carcinomatosis is the typical manifestation of metastases and is seen in approximately 75% of cases.<sup>53</sup> Less common manifestations of metastases in treated ovarian cancer are the lymph nodes, lungs, pleura, and liver parenchyma.<sup>52,53</sup> Unusual and rare types of recurrence including isolated distant, central nervous system manifestations, bone, skin, or soft tissue metastases tend to occur late in the disease.<sup>54</sup>

CT has been widely used for assessing suspected recurrence in patients treated for ovarian cancer. Complementary PET/CT is mostly performed in patients with unremarkable or equivocal CT findings but rising tumour markers. A systematic review reported that contrast-enhanced PET/CT has a pooled sensitivity and specificity of 93.94% and 93.80%, respectively, for detecting recurrent disease.<sup>55</sup> Apart from whole body assessment, advantages of PET/CT include the depiction of small size metastases or metastases at sites difficult to assess with CT, e.g., of the bowel surface, mesentery, or subtle lymphadenopathy. However, microscopic peritoneal recurrence or lymph node metastases with a diameter of less than 5 mm are also beyond the detection of fluorodeoxyglucose-PET/CT.<sup>56</sup>

In patients treated for ovarian cancer, imaging renders pivotal information for tailored treatment planning in multidisciplinary boards. It ascertains the presence of suspected recurrence and demonstrates their site and tumour load. It also

provides other important information such as potential complications of treatment.<sup>53</sup> Imaging also renders crucial information for selecting candidates eligible for cytoreductive surgery. In these patients, distant metastases as well as irresectable local disease have to be excluded. In this scenario PET/CT is superior to CT to demonstrate small or distant metastases.<sup>57</sup>

It is optimally combined with MRI, as this presents the single best modality for local surgery planning, e.g., the pelvic sidewalls or other important structures.<sup>5</sup> Advances in the management of ovarian cancer recurrence are to be expected when PET/MRI will become more widely available in clinical practice.

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# An Epidemiological Study on Paediatric Brain MRIs with a Focus on Contextual Reporting



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## Abstract

**Objectives:** Paediatric neuroradiology is one of the most challenging areas in the wide gamut of disciplines that modern radiology encompasses. There is a paucity of literature on the epidemiology of paediatric neuroimaging and contextual reporting in this field. The objectives of this study were to study the epidemiology of the paediatric neurological disorders and to study the role of contextual reporting in this field.

**Materials and methods:** This study was conducted at a tertiary care center in South-Western India over 1 year. It was a retrospective epidemiological study. The authors studied 112 patients referred as in- or outpatients for a brain MRI for a wide range of indications. The authors analysed the reports issued by their radiologists and reformatted them into a newly proposed contextual reporting template for the paediatric brain. Then, the authors conducted an epidemiological analysis of the compiled data.

**Results:** The authors found that the most common indication for paediatric neuroimaging was seizures or seizure-like episodes, followed by developmental delay. The most common abnormality on imaging was sequelae to hypoxic or hypoglycaemic insult followed by brain atrophy. The authors found a wide range of other abnormalities illustrating the wide spectrum of paediatric neuroradiology.  
**Conclusion:** The authors study fills a gap in current literature regarding the epidemiology of conditions encountered in paediatric neuroradiology. The authors also propose a novel reporting format for contextual reporting in this field, which may help in reducing errors in reporting and reduce reporting time.

## Key Points

1. Challenges in capturing reliable paediatric neuroimaging mean that accurate reporting is imperative. A better understanding of epidemiological breakdown of indications for neuroimaging can help to direct accurate reporting, particularly when using 'contextual reporting' methods.

2. This retrospective epidemiological study found that the most common indication for paediatric neuroimaging was seizures or seizure-like episodes, followed by developmental delay. The most common abnormality observed on imaging was sequelae to hypoxic or hypoglycaemic insult, followed by brain atrophy.

3. Contextual reporting of paediatric neuroimaging, where the structured reporting format is dependent on clinical indication, may improve the speed and accuracy of reporting. The authors of this study provide a suggested template for contextual reporting in paediatric neuroimaging.

## INTRODUCTION

Paediatric neuroradiology is one of the most challenging areas in the wide gamut of disciplines that modern radiology encompasses.<sup>1</sup> There are numerous challenges to obtaining diagnostic quality images, which range from inherent poor signal-to-noise ratio to patient motion to the rapid changes, which are happening in the developing paediatric brain.<sup>2</sup>

There is a paucity of literature, particularly in the Indian population, on the spectrum of paediatric brain disorders and the value of MRI in their diagnosis. There have been multiple epidemiological studies on specific disease groups, including paediatric brain tumours and neonatal seizures.<sup>3,4</sup> However, the authors could not find a study analysing the entire spectrum of neuroimaging findings in this age group. Hence, the primary aim of this study was to dissect the epidemiology of paediatric brain disorders on neuroimaging in a tertiary care center.

Contextual reporting is an alternative way to report where the reporting format is dependent on clinical indication.<sup>5</sup> This approach is finding increasing traction in recent literature.<sup>6</sup> The authors explore the role of contextual reporting in paediatric neuroimaging. The authors also endeavor to suggest tailored study protocols, as well as a fresh format for contextual reporting for different indications in paediatric neuroimaging to, increase the speed and accuracy of reporting. Hence, this study had two aims; first, to provide an epidemiological distribution of paediatric brain conditions seen on neuroimaging and second, to

create a comprehensive template for contextual reporting of the paediatric brain MRIs.

## METHODS

### Study Population

A total of 112 paediatric patients ranging from 0–18 years of age as per the World Health Organization (WHO) definition of a paediatric patient were studied retrospectively from 01 May 2019–31 April 2020.<sup>7</sup> These were various inpatients or outpatients who were referred for MRI of the brain for a wide range of indications. The authors included all patients fulfilling these criteria. Most of the patients were examined once during the study period except for a few who underwent follow-up studies. The authors excluded these follow-up studies from the study.

### Initial Clinical and Laboratory Evaluation

In addition to the clinical details provided on the requisition forms, detailed perinatal history was collected for all the patients. This included the history of pre-term or post-term delivery, birth asphyxia, admission to neonatal intensive care unit, and history of meconium aspiration. Relevant biochemical and genetic test results were recorded for all the patients. As an institutional protocol, this data is collected and recorded from all patients visiting the MRI centre by interviewing the patients or caregivers and

reviewing their documents. The same data was used for this study. Also, the following data were recorded for all patients: age, sex, symptoms, age of their onset, examination findings, and provisional clinical diagnosis.

### Equipment and Technique

The MRI examination was performed using a 1.5T Siemens Somatom Symphony MRI machine (Siemens AG, Munich, Germany). The authors followed the institutional magnetic resonance (MR) protocol for brain imaging, which included T1-weighted (W), T2W, T1W inversion recovery, fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging, and gradient-recalled echo sequences in the axial plane (T2W sequence in the coronal plane and T1W sequence in the sagittal plane). In selected cases, 3D-T1W- magnetisation-prepared rapid gradient echo imaging, fat-saturated post-contrast imaging, MR angiography, MR spectroscopy, and constructive interference in steady state sequences were employed based on the clinical history and imaging findings on routine sequences. A few patients also underwent simultaneous imaging of the spine.

All MRIs were reported by different radiologists (eight in total) out of which one was a neuroradiologist. The authors included all radiologists in their institute with experience ranging from 2–18 years. Many of the cases were discussed in intra-departmental conferences. The template used for reporting was the same as the adult template with additional remarks on the degree of myelination.

### Data Analysis

During data analysis, the authors analysed the narrative reports issued by their radiologists. The authors then reformatted these reports into a newly proposed contextual reporting template for the paediatric brain. The authors designed a fresh template that was inspired from the work of Mamlouk et al.<sup>8</sup> Mamlouk et al.<sup>8</sup> have suggested four different formats for contextual reporting in the paediatric brain. However, the authors used the spectrum of findings seen in this study

to build a single fresh comprehensive template (Table 1), which can serve as a one-stop-shop for reporting these cases. The authors performed statistical analysis of patient age using MedCalc Statistical Software version 14.8.1 (MedCalc Software, Ostend, Belgium). Descriptive statistics are presented in frequencies and percentages for categorical variables. For continuous variables, means, and standard deviations summarise normally distributed data, while medians and ranges summarise non-normally distributed data.

### Ethical Considerations

The study was performed in a manner to conform with the Helsinki Declaration of 1975, as revised in 2000 and 2008, concerning human and animal rights, and the authors followed the policy concerning informed consent. The study was approved by the Institutional Ethics Committee (IEC) of the corresponding authors' institute. The parents or caregivers of the children reported in this article had signed a written informed consent form. This study was conducted in a medical educational centre, in which all patients are informed that they may be subjects of scientific experiments and are informed of the ethical codes of conduct. This was a retrospective study without active intervention and no enrolment in the public trials registry was required as per the ethical code of conduct of their institute.

## RESULTS

### Patient Demographics

The study population ranged from age of 7 days–17 years, with a median age of 6.5 years. There was a predominance of male patients (n=70) compared to female patients (n=43).

### Clinical Parameters

In the patient population, 103 patients were born at term, eight were pre-term, and only one patient was delivered post-term. A total of 17 patients had a history of neonatal intensive care unit admission ranging from 3–21 days. Among these were five patients were born pre-term and one was born post-term. A total of 13 patients had a history of birth asphyxia.



Table 1: Proposed contextual format for reporting paediatric brain MRI.

Contextual format for reporting paediatric brain MRI	
Age	
History	
Technique	
IV contrast administered	
Special MR sequences (if any)	
Comparison	Date of prior examination/not available
Brain parenchyma: <ul style="list-style-type: none"> <li>• Volume</li> <li>• Infarct</li> <li>• Haemorrhage</li> <li>• Lesions</li> <li>• Malformations</li> <li>• Midline structures including the corpus callosum</li> </ul>	
Myelination	
Ventricles	Size: normal/enlarged
	Margins: sharp/wavy
Thalamus and basal ganglia	
Sella and pineal region	
Brainstem	
Cerebellum: <ul style="list-style-type: none"> <li>• Hemispheres</li> <li>• Vermis</li> <li>• Tonsils</li> </ul>	
Collections	None/intra-axial/extra-axial
Vascular abnormality	
Calvarium	
Special sequences	
Others	
Provisional diagnosis	
Differential diagnosis	
Advice for further investigations or follow-up imaging	

IV: intravenous; MR: magnetic resonance.

The most common indication for imaging was focal or generalised seizures or seizure-like episodes in 31 patients. This was followed by the developmental delay seen in 28 patients. This included global developmental delay, intellectual disability, loss of acquired milestones, or short stature. Twenty seven patients presented with haemiparesis or cerebral palsy. A total of 23 patients were grouped under miscellaneous, which included patients presenting with headache, patients on follow-up for malignancies and tuberculosis, patients undergoing brain screening to rule out metastases, and patients with a syndrome. Two patients were suspected of having tuberous sclerosis. None of the patients in the study had undergone genetic or enzymatic studies before imaging.

### MRI Findings

The authors analysed the existing reports issued by the radiologists to extract key headings from them. Following this, the authors created a contextual reporting template to attempt an improvement upon one suggested by Mamlouk et al.<sup>8</sup> The format prepared and used by the authors is detailed in [Table 1](#).

### Brain Parenchyma

#### Parenchymal volume

The authors found 22 patients to have various degrees of diffuse brain atrophy. One patient had unilateral atrophy of the left cerebral hemisphere. Another patient had unilateral atrophy of the hippocampus.

#### White matter abnormalities

A total of 27 patients had white matter abnormalities. The most common finding was the presence of abnormal T2/FLAIR white matter hyperintensity. This was most commonly seen in the periventricular region (in 16 patients) and was associated with a paucity of white matter-suggestive of periventricular leukomalacia (PVL). Two of these patients also had FLAIR hyperintensities in peri-rolandic regions. One patient had isolated involvement in the peri-rolandic region. One patient was

found to have cystic PVL. Two patients showed white matter hyperintensities, with the corresponding restriction of diffusion. Based on clinical findings, one of these was suspected to be acute demyelination, whereas the findings were presumed to be due to hypoxic white matter injury in the second patient. These were the primary differential diagnoses offered by the reporting radiologists after clinic-radiological correlation. A total of four patients showed asymmetrical white matter hyperintensities, which followed no particular patterns and were suspected to be sequelae of seizures or demyelination. One patient showed radial migration lines and was confirmed to have tuberous sclerosis.

#### Infarcts

The authors found one patient with acute infarcts and 10 patients with chronic infarcts. The middle cerebral artery territory was the most commonly involved vascular territory.

#### Haemorrhages

There was only one case of right periventricular haemorrhage. This patient also had cortical laminar necrosis in bilateral peri-rolandic regions. Two of the patients had haemorrhagic cortical contusions with a history of preceding trauma.

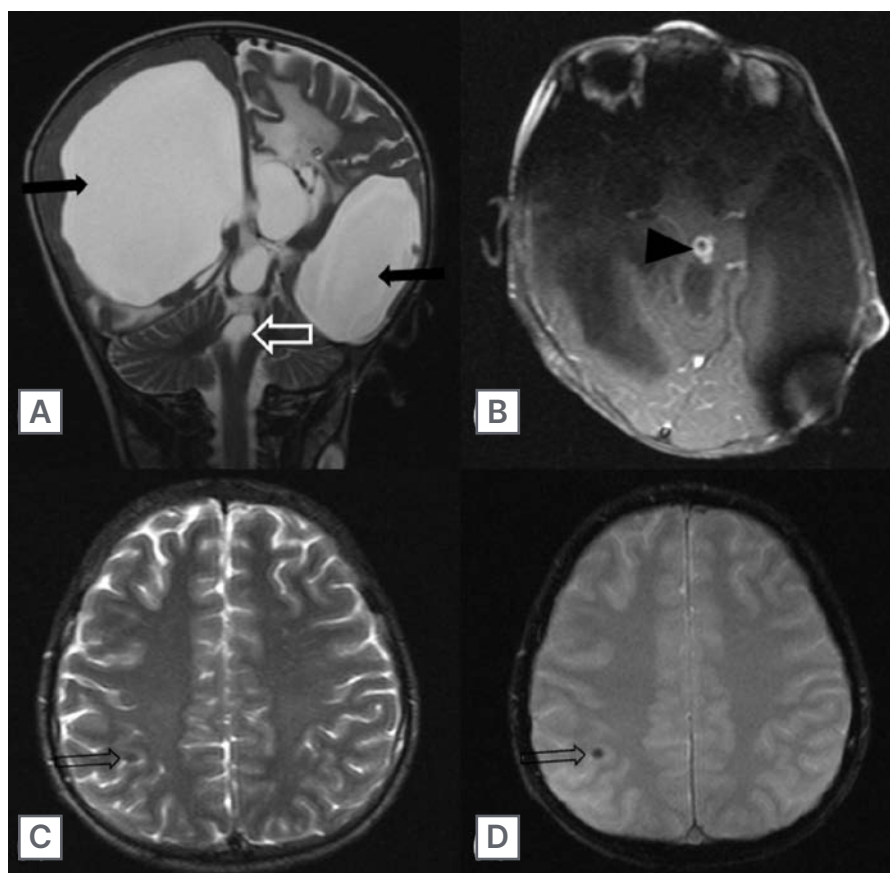
#### Focal lesions

Four patients had intraparenchymal lesions. Two of these had multiple ring-enhancing lesions ([Figures 1A and 1B](#)) and one had a calcified lesion in the right parietal lobe, which likely represented a calcified granuloma ([Figure 1C and 1D](#)). One patient had periventricular calcifications with associated findings representing congenital *cytomegalovirus* infection.

#### Malformations

The study population had six patients with structural malformations. Two of them had cortical tubers and turned out to have tuberous sclerosis. One patient had Type II focal cortical dysplasia with nodular heterotopia. The other three patients had ulegyria, lissencephaly, and pachygyria polymicrogyria complex respectively.

Figure 1: Spectrum of intracranial infections.



A) This MRI brain of a 1-year-old male shows the presence of gross dilatation of bilateral lateral ventricles and third ventricle (solid black arrows), with normal-appearing fourth ventricle (white void arrow) on T2W coronal images, suggestive of non-communicating hydrocephalus.

B) A T1W post-contrast axial image shows an enhancing nodular lesion in the midbrain (black arrowhead).

C) A MRI brain image in a 15-year-old male, who presented with seizures, show a punctate focus of hypointensity (void black arrow) on T2W axial.

D) Gradient echo axial images, which is likely to represent a calcified infective granuloma.

W: weighted.

### Midline structures

All 22 patients with diffuse brain atrophy had various degrees of associated corpus callosum atrophy. Besides, two patients had corpus callosum atrophy with preserved brain volume. One of them had associated lissencephaly, whereas others had findings representing PVL.

### Myelination

There were four patients with abnormal myelination, which did not correspond

to their age. One of these had delayed myelination in the frontal and parietal white matter along with diffuse cerebral atrophy. Another patient had findings representing hypomyelination (T2 hyperintensity of white matter, with a relatively normal signal on T1W image) at the age of 7 years. The other two patients, aged 12 and 5 years, had diffuse white matter signal abnormality, with the onset of symptoms at age of 4 and 2 years, respectively, leading to a provisional diagnosis of a demyelinating disorder.

## Ventricles

In the study population, 11 patients had ventricular abnormalities. Five of these had a communicating pattern of hydrocephalus, with causes ranging from Chiari II malformation to congenital *cytomegalovirus* infection. One patient had a ring-enhancing lesion in the mid-brain leading to aqueductal stenosis and resultant obstructive hydrocephalus (Figures 1A and 1B). One patient with a history of trauma had an intraventricular haematoma. Two patients had asymmetric ventricular dilation after placement of ventriculoperitoneal shunt. Interestingly, one of these had multiple 1–2 mm sized enhancing lesions along the ventriculoperitoneal shunt in the left parietal lobe, which likely represented foreign body granulomas. Lastly, two patients with tuberous sclerosis in this study had subependymal nodules.

## Thalamus and Basal Ganglia

The authors found six patients with a varying spectrum of findings in basal ganglia. Three of the patients had gliosis and encephalomalacia. One patient had a haemorrhage in the right thalamus, whereas another patient showed restriction of diffusion in bilateral thalami and basal ganglia (with similar findings in white matter due to hypoxic injury). The last patient had calcification in the right basal ganglia, which in conjunction with his other findings, led to the diagnosis of congenital *cytomegalovirus* infection.

## Sella and Pineal Region

The authors found two patients with sellar abnormalities. The first patient with a known case of Langerhans cell histiocytosis, had a loss of posterior pituitary bright spot. The second patient had partial empty sella. No abnormality of the pineal region was seen.

## Brainstem

The authors found one patient with gliotic changes in the vascular territory of the right superior cerebellar artery, representing the sequelae to previous ischemic insult. Another patient had a ring-enhancing lesion

in the mid-brain leading to hydrocephalus, as described above (Figures 1A and 1B).

## Cerebellum

Previously described 22 cases of diffuse cerebral atrophy also showed various degrees of cerebellar atrophy. Also, one patient had isolated severe cerebellar atrophy and was suspected to have neuronal ceroid lipofuscinosis. One patient with Chiari II malformation had low-lying peg-shaped tonsils and another patient had tonsillar ectopia without additional abnormalities. No abnormalities of the cerebellar vermis were seen.

## Collections

One patient had epidural and subdural collections showing restriction of diffusion and representing abscesses. Another patient with a history of trauma had a subdural haematoma.

## Calvarium

The authors found three patients with microcephaly and another patient with occipital bone osteomyelitis.

## Special Sequences and Screening of Neuraxis

The authors performed MR angiography, MR venography, single-voxel MR spectroscopy, and T1, T2, and short tau inversion recovery sagittal sequences for the screening of spinal cord in selected cases. These sequences did not reveal any significant findings.

## Other Findings

The miscellaneous findings were found in 15 patients and included entities such as cavum septum pellucidum (n=2), mega cisterna magna (n=3), otomastoiditis (n=1), pansinusitis (n=1), encephalocele (n=1), scalp haemangioma (n=1), and cleft palate (n=1). The patient with elongated and tortuous intracranial vessels was suspected to have Menkes disease.



### Provisional Diagnosis

The authors had 41 cases with an impression of 'normal study' or 'no significant abnormality'. The remaining 81 cases had a wide spectrum of provisional diagnoses. These are listed in the pie chart in Figure 2.

### DISCUSSION

Paediatric neuroimaging continues to pose enormous challenges to radiologists across the spectrum from trainee residents to consultants. There are few studies citing workload devoted to paediatric neuroimaging in tertiary care setups. Cowan et al.<sup>9</sup> reported that paediatric neuroimaging makes up for around 3% of total MRI examinations.

There have been few studies on the epidemiological distribution of paediatric brain conditions on neuroimaging. Most of these are focused on selective groups of diseases like brain tumours, epilepsy, or neural tube defects.<sup>3,4,10</sup> This study tries to fill this information gap by providing a breakdown of all the paediatric brain conditions seen on imaging. This would assist in better

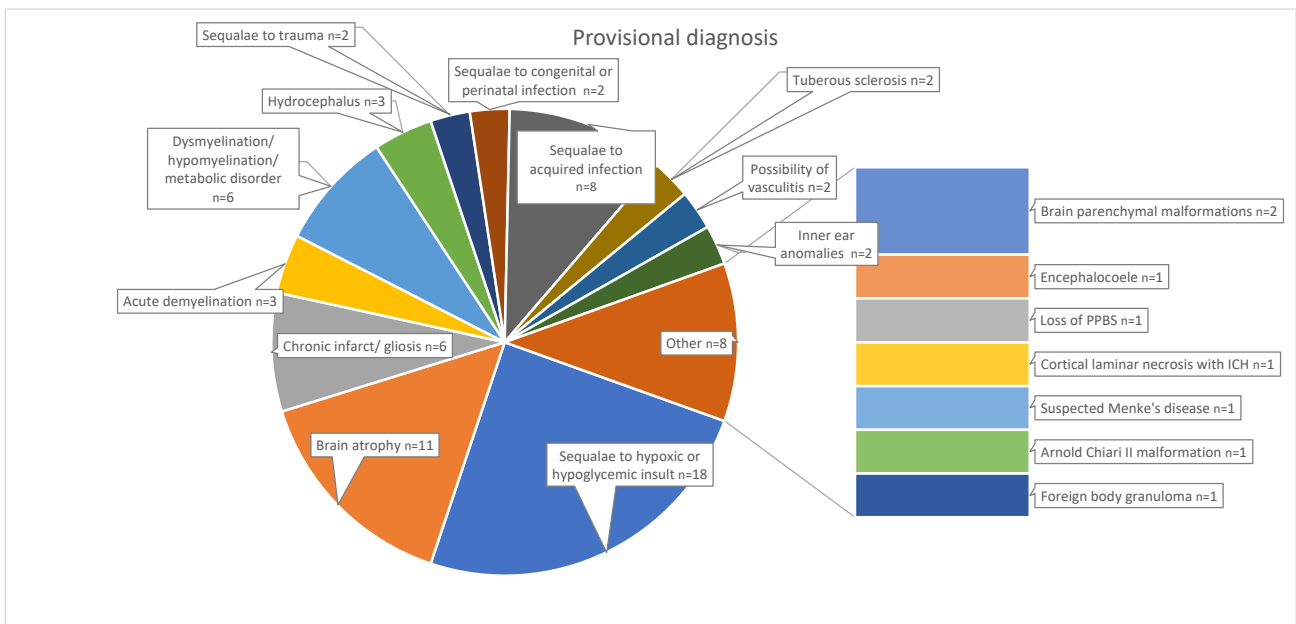
understanding of the incidence and distribution of various MRI findings in paediatric neuroimaging.

The most common finding in the analysis was the presence of features of hypoxic or hypoglycemic brain injury seen in 16% of the study population. The authors grouped these two entities together as there is a wide overlap in imaging findings of these conditions. The reported incidence of hypoxic injury in the literature ranges from 2–6 per 1,000 live births.<sup>11</sup> The authors study reflects a higher incidence which can be attributed to the fact that they only included children referred for neuroimaging.

This was followed by the presence of brain atrophy in 9.8% of the study population without any other abnormality. This a known phenomenon that many paediatric patients show brain atrophy without other clues on MRI. This group usually has a high probability of genetic abnormalities.<sup>12</sup>

Another objective of this study was to explore the role of contextual reporting in this field. This was achieved by breaking

Figure 2: Provisional diagnoses in the study population.



ICH: Intracerebral haemorrhage; PPBS: posterior pituitary bright spot.

down the existing reports to extract their key findings and then using them to design a fresh template that can be used across all cases of paediatric neuroimaging. Contextual reporting is a form of structured reporting that entails using a reporting format that is tailored towards a particular disease or related group of diseases.<sup>8</sup> This differs from structured reporting where reporting formats are set for a particular organ system. Contextual reporting provides focused content related to the particular disease and offers a 'checklist' for all pertinent points required to answer the clinical question.<sup>13-15</sup>

The inherent challenges in paediatric neuroimaging render it near impossible to perform additional imaging in the event of a missed finding on the preliminary review (while the scan is going on). The primary reason for this is a need for general anaesthesia or heavy sedation in most of the cases for performing MRI.<sup>2,16</sup>

For example, if a small lesion is missed in the sella during the preliminary review and the scan is completed without administering the contrast, a repeat scan may be required to evaluate contrast uptake of the lesion. Although MRI is a non-ionising modality, such a scan requires repeat sedation, which has its own inherent risks.<sup>17</sup> This makes it imperative that radiology trainees use a standardised format for the preliminary review of the images while the patient is inside the gantry. This would also help in adding sequences tailored to a particular condition. This approach has been shown to reduce error rates and reduce reporting times.<sup>18</sup>

Mamlouk et al.<sup>8</sup> have done pioneering work in creating around 50 templates for reporting

in neuroradiology. The authors selected paediatric neuroradiology from this wide spectrum for the reasons discussed above. The authors suggest a contextual reporting template for paediatric brain imaging to attempt and further improve upon their work (Table 1).

The authors template covers a wide range of possible abnormalities encountered in paediatric neuroradiology. The authors used the spectrum of findings in this study to build a comprehensive format that can serve as a one-stop-shop for reporting these cases. The contextual reporting format also enables the treating physician by presenting the findings in a structured format. This would help in patient management.

The authors acknowledge the limitations of this study in the form of a relatively small sample size, lack of follow-up examinations for the study group to evaluate the temporal change in studied parameters, and the lack of genetic data. The authors consider this study to be one of the building blocks in the rapidly emerging trend of contextual reporting. In the future, these templates can be integrated with clinical, biochemical, and genetic data leading to data integration and improved patient management. These templates also enable epidemiological research and deep learning.<sup>19,20</sup>

## CONCLUSION

In conclusion, this study fills a gap in current literature regarding the epidemiology of conditions encountered in paediatric neuroradiology. The authors also propose a novel reporting format for contextual reporting in this field, which may help in reducing errors in reporting and the reporting time.

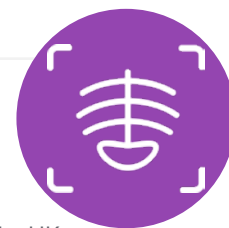
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# Percutaneous Nephrostomy Insertion Training: An Overview



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## Abstract

Percutaneous nephrostomy insertion is a technique performed by an interventional radiologist or a urologist for an acutely or long-standing obstructed urinary tract. Mastering the technique involves overcoming a steep learning curve. Various methods of training have been developed over the years to facilitate learning. These vary from simple physical models, such as biological or non-biological practice phantoms, to more sophisticated virtual reality sets, which allow for a more lifelike learning environment by replicating factors such as kidney movement caused by breathing. The authors discuss the pros and cons of different practice models and challenges that trainees face on their journey to becoming competent at performing nephrostomies. They also propose their recommendations based on the experience of trainees in their institution.

## Key Points

1. Percutaneous nephrostomy insertion is a highly effective, low-risk technique performed by interventional radiologists or urologists. Different methods of training exist, using both *in vivo* and *ex vivo* techniques.
2. Hybrid *ex vivo* models of training, used in conjunction with traditional teaching, can achieve greater competence and confidence in trainees in a shorter space of time than could ever be achieved with conventional *in vivo* training.
3. *Ex vivo* training tools can not only increase early exposure to the steps of percutaneous nephrostomy in a safe, risk-free environment, but can be used to train greater numbers of trainees than *in vivo* cases can.



## INTRODUCTION

Urinary tract obstruction is a common acute presentation to secondary care. Relief of upper urinary tract obstruction is usually performed in acute cases, or in chronic obstruction where treatment of the causative process is not immediately possible. Common benign causes for an acutely obstructed renal tract are renal calculi, pelvic ureteric junction obstruction, and retroperitoneal inflammatory or fibrotic processes. Chronic obstruction may be due to pelvic malignancy, pregnancy, or urothelial strictures.

Percutaneous nephrostomy (PCN) is a commonly performed procedure for the decompression of an obstructed urinary system. First described in 1955, it has since been widely adapted with a good success rate, low complication rate, and without the need for general anaesthesia.<sup>1</sup>

Formal curriculum advice regarding the skill of percutaneous renal access for both radiology and urology trainees is widely variable, and currently implemented restricted working patterns have a limiting impact on surgical training opportunities.<sup>2</sup> The authors discuss the challenges faced by trainees in gaining exposure to PCN insertion, and detail some of the options available to enhance training.

## PERCUTANEOUS NEPHROSTOMY: WHO DOES IT AND HOW?

In the UK, PCN is a core competency, as recognised by the Royal College of Radiologists (RCR), for higher interventional radiology trainees. In most cases, percutaneous renal access is obtained by radiologists. In comparison, in Europe, both radiologists and urologists are trained in percutaneous access. Increased exposure and training in both ultrasound skills and PCN in the core urology curriculum would undoubtedly alleviate the pressure on interventional radiologists, as well as provide urologists with an ability to perform endourological procedures independently.

Access to the renal system is achieved by image guidance, with multiple modalities available. Initial needle puncture is commonly performed under ultrasound guidance, and subsequent

intervention to the urinary tract can be carried out under ultrasound or fluoroscopic guidance. Fluoroscopy enables the operator to visualise the upper renal tract in real-time with an option to image from different angles, allowing for easy assessment of the position of interventional wires and catheters used during the procedure. PCN can be performed in conjunction with the insertion of J stents, and cases are usually collaborated and discussed between radiologists and urologists in regard to the preferred order of intervention. It is also the initial step that allows access to the upper renal tract in common urological procedures, such as percutaneous lithotripsy.

## COMPLICATIONS OF PERCUTANEOUS NEPHROSTOMY

PCN is a highly effective and relatively low-risk procedure. A study describing the safety profile of PCNs performed by radiologists conducted on large numbers of patients reported success rates as high as 98%, with a relatively low complication rate of 6.5%.<sup>3</sup> Similarly, high success rates and low complication rates have been reported in various countries, including Sweden, Pakistan, and the UK.<sup>4-6</sup>

Reviews of patient outcomes after PCN tube insertion done by urologists are equally favourable. In a retrospective analysis of 650 percutaneous nephrostomies carried out over a 10-year period by both urology consultants and registrars, Skolarikos et al.<sup>7</sup> found similarly high technical success rates of 96% and 93%. Major complication risks were also found to be low: 3.6% for registrars and 3.1% for consultants.

Potential complications are rare, albeit possible. These are frequently classed as early (such as sepsis, retroperitoneal haematoma, bleeding, solid organ injury, and urinoma) or late (for example, catheter blockage or dislodgement). Reported complication rates for radiologists as well as urologists are relatively low, without major discrepancies between the two groups.<sup>5</sup>

Review of data from the contemporary UK setting yields congruent findings. Armitage et al.<sup>8</sup> conducted the first UK national comparison of outcomes of percutaneous nephrolithotomy (PCNL), obtained by urologists versus

interventional radiologists. They found that of the 5,211 procedures that were done between 2009 and 2015, 66.3% were carried out by interventional radiologists. They found no major patient outcome differences between the two groups, and favourable results were achieved regardless of whether the procedure was done by a urologist or an interventional radiologist. Interestingly, the authors noted some differences in practice between the two groups, such as the much higher use of ultrasonography by radiologists, and a higher rate of supine punctures performed by urologists.

Studies have shown that there is a correlation between the operator's experience level and the post-procedure complication rate. A 10-year review found that inexperienced operators (those who had performed less than 20 PCNs, with a mean of 5.6) were found to have a 17% complication risk. Bleeding and urinary leaks were the most common problems. Of the patients who had PCN performed by experienced operators (at least 20 prior procedures, with a mean of 178 cases), only one required a further intervention for their complication, whereas the less experienced operator group had 10 patients who required a repeat procedure.<sup>9</sup>

## METHODS OF TRAINING

In the past, experiential learning underpinned surgical training. The ability to perform procedures under close supervision, with feedback from senior clinicians, was the only available method for trainees to progress in training. Factors such as increasing demand, pressures on operating and interventional rooms, and fear of litigation make this approach less favoured nowadays.<sup>10</sup> Learning of any new procedural skill always starts with the acquisition of knowledge and the theory that underpins it. Equally important is the experience; in the hands of an inexperienced operator, PCN is a potentially risky task, with potential for complications. As such, there is a real need to be able to simulate PCN to allow trainees to practice. Many such methods for training already exist. Here, the authors discuss the pros and cons of methods put forward as means of training junior radiologists and urologists in PCN and renal access.

## Simulation-Based Training

Simulation has been a common method of training. It is already a well-established method of training in aviation, where, understandably, training *in vivo* would be high-risk. Methods vary from simple physical models to more sophisticated virtual reality (VR) sets, where computerised technology is used to mimic variable anatomical and real-life factors, such as respiratory movement of the kidney. They can also provide real-time feedback by measuring predetermined factors, such as the dose of radiation used during the simulation.<sup>11</sup>

Simulation allows trainees to repetitively practice a skill in a pressure-free environment. It allows theoretical knowledge obtained out of the classroom to be applied safely into practice, as well as for mistakes to be made in a controlled, safe environment, where direct feedback can be obtained. Based on the fidelity, simulators can be classified into two categories: low-fidelity (suturing pads) and high-fidelity simulators (Harvey cardiology manikin). Simulator fidelity must be considered when developing simulation programmes. Rudolph et al.<sup>12</sup> suggested that three features of simulation fidelity influence the overall experience of the learner. These are physical fidelity (physical attributes of the equipment and environment), conceptual fidelity (the actions and events make sense), and finally, experiential and emotional fidelity (the holistic experience, including the emotions and cognitive states of the participants). The impact of simulation fidelity on learning outcomes may vary, based on the trainees and training goals. It is possible that a low-fidelity model would be acceptable to accomplish modest improvements for novices learning the task, but not mastery. It is therefore important to consider both fidelity and instructional design before planning a training course.

## Benchtop Models

More accessible benchtop models exist and these can be both biological (often consisting of a porcine kidney within a mould) or non-biological. The main pros of benchtop models over wet-lab models are the ease of set-up, and the ability to practice repetitively (Figure 1A). These benchtop models are also cheaper than more high-tech simulators.<sup>13</sup>

## Phantom Models

Benchtop phantom models are another modality of training used in other factions of surgical and radiological training, from basic suturing skills to more advanced vascular interventions. A study conducted at the Department of Urology, University of California, San Francisco, California, USA, found that confidence with percutaneous renal access increased after the use of a phantom model for training, alongside direct senior clinician feedback. Fifteen urology trainees were divided into three groups, and underwent time trials on a phantom model for percutaneous renal access. Group 1 were given access to the phantom model prior to time trial; Group 2 were given a teaching session on renal access by a senior clinician, followed by access to the phantom; and Group 3 were given a teaching session and access to the phantom for practice, in addition to individual feedback from a senior clinician whilst using the phantom prior to the time trial. The results of this study demonstrated that urology trainees in Group 3 demonstrated the greatest improvement in technical skills assessed, including the number of attempts to gain renal access, accuracy of needle puncture, and time to needle placement.<sup>14</sup> Although nephrostomy and renal access phantoms have their benefits in training, the cost can limit availability across training schemes. Rock et al.<sup>15</sup> submitted an easily reproducible and cheap gelatin-based phantom model to the British Society of Radiology (BIR) in 2010. They suggested that a hydronephrotic collecting system could be replicated by a fluid-filled and tied-off disposable vinyl glove. Gelatin surrounding this simulated kidney was used to replicate the renal parenchyma. This was then inserted into a plastic bottle split mould, and refrigerated to simulate a hydronephrotic kidney. It was subsequently inserted longitudinally into a gelatin-filled plastic box, and cooled again to create the final phantom model, in which ultrasound-guided PCN could be simulated, including the ability to aspirate fluid to confirm needle placement. Although not statistically supported, this is an example of how benchtop phantoms can be easily and cheaply reproducible, to allow *ex vivo* training opportunities.<sup>15</sup>

The SimPORTAL C-arm Trainer contains a flank model with an anatomically accurate cast of the pelvicalyceal system and the ureter, with

an overlay of ribs for needle puncture, and a mini C-arm for fluoroscopic simulation, with two mounted video cameras. Approximately 92.8% of the 14 enrolled participants considered the SimPORTAL C-arm Trainer of at least equal value to existing VR training models.<sup>16</sup> Using the SimPORTAL model, Poniatowski et al.<sup>17</sup> showed that average maximum forces for needle puncture into skin varied from 2.75 N to 2.80 N for human tissue, and from 4.53 N to 4.19 N for simulated human tissue.

There is evidence that hybrid *ex vivo* models of training with benchtop models used in conjunction with traditional senior-led teaching, direct supervision, and feedback on trainee performance can achieve greater competence and confidence in trainees in a shorter space of time than could ever be achieved with traditional *in vivo* training. A common drawback of these types of models is their inability to replicate the human factors involved with PCN (e.g., movement of the kidney with respiration and the true tactile experience of puncturing the flank and entering the perinephric space).

## Augmented Reality and Virtual Reality

A prospective study performed by Papatsoris et al.<sup>18</sup> looked at the impact of VR training of percutaneous renal access in a cohort of 36 urology trainees who had never performed the procedure before. The PERC Mentor™ (3D Systems [formerly Symbionix USA Corp.], Rock Hill, South Carolina, USA) was initially used by a consultant urologist to demonstrate renal access puncture and guidewire access (Figure 1A and 1B). This simulator mimicked percutaneous renal access with a 3D model of the patient's flank, a virtual fluoroscopic C-arm, and pedals which simulated fluoroscopic screening. Ports allowed the introduction of guidewires and catheters into the simulator. The trainees were then given two 1-hour sessions, a week apart, on the simulator device, as well as a report of the statistics on their performance, such as procedural time, radiation exposure, volume of contrast used, and potential complications. This study found that the use of simulation was statistically significant in reducing the amount of radiation used by the trainees, as well as the time taken to perform the procedure. In addition, the time to gain desirable guidewire placement was halved after training. The PERC Mentor has been evaluated

**Figure 1: An example of a commercially available benchtop model available for percutaneous nephrolithotomy training.**



A) Samed PCNL Training Device LS40 bench-top model;  
 B) PERC Mentor™ (3D Systems [formerly Symbionix USA Corp.], Rock Hill, South Carolina, USA); flank pad;  
 and  
 C) Display monitor PERC Mentor™.

well, and face, content, construct, predictive validities, and skill acquisition by trainees have been reported.<sup>19-21</sup> The cost of the simulator (100,000 USD) is the main reason for the lack of widespread acceptance.

The K181 VR surgical simulator (Marion Surgical, Niagara Falls, Ontario, Canada) allows users to interact with a virtual patient in a virtual operating room (Figure 2). The system has three main components: the VR headset places the user in a virtual operating room, and the haptic system offers the user with haptic force-feedback calculated by the tissue simulator. Twelve participants evaluated the simulator, and 95% reported realistic renal access simulation.<sup>22</sup>

Augmented reality (AR) and VR simulators offer additional features such as the ability to recreate a number of pre-programmed scenarios that may be encountered in practice but cannot be replicated with a benchtop model. These may help expose trainees to a range of potential complications, and allow for the practice of dealing with these when encountered in reality. The only other method of training that has shown evidence of helping trainees to deal with complications is live anaesthetised animal models, which are not often used in the UK because of ethical reasons. Levels of procedural

difficulty can also be manipulated in AR and VR to allow for the development of not only basic technical skills, but also more advanced procedural skills, and confidence in a variety of scenarios. VR and AR allow for statistical analysis of performance, which can aid the training circle by providing ongoing feedback to the trainee, and evidence of progression in obtained skills.<sup>23</sup>

The Perk Tutor (Queen's University, Kingston, Ontario, Canada) AR training system is used for teaching and assessing PCN using tracked-ultrasonography-snapshot (TUSS) technology. Four novice urology residents with no prior experience in PCN participated in a study as operators, and each operator completed two TUSS-navigated procedures and two conventional ultrasonography-guided procedures. TUSS-guided PCN was noted to be superior in several parameters, including the number of attempts, time taken, and amount of needle motion in tissue. The model is not commercially available due to lack of validation.<sup>24</sup>

### Live Anaesthetised Animal Studies

Studies that analysed live animal models have shown that most aspects of the real-life PCN procedure can be successfully replicated, adding a sense of realism to the training. Live



Figure 2: Marion Surgical K181 Simulator (with permission from Marion Surgical, Niagara Falls, Ontario, Canada).



porcine models have been rated as superior to simulators in terms of realism, movement of the kidney, and tactile feedback in studies.<sup>25</sup> As with most biological methods of training, the main drawbacks are the limited use and inability to be used repetitively. In most UK institutions, use of live animals is difficult for ethical reasons.

### Cadaveric Training

Cadaveric training, although a staple method of training in other aspects of surgical training, has few percutaneous access studies validating its effectiveness. It is a limited resource, and is not often widely available across different training sites. In addition, cadaveric methods of training do not provide haptic feedback, which is often essential in percutaneous intervention.

### PROBLEMS FACED BY TRAINEES

Doctors in training who wish to learn nephrostomy tube insertion are certain to face a number of challenges. Increasing trainee numbers limits the number of learning opportunities during daytime working hours, and contemporary working patterns may be an obstacle in gaining hands-on experience outside of contracted hours.

Some of the teaching methods (e.g., simulators), although generally well-received, come with their own limitations (Table 1). Their availability

to trainees varies between hospitals and access can be limited. Furthermore, their actual usefulness remains to be proven. Simulators can certainly fill learning gaps in the initial stages of training, where trainees have no prior experience of the procedure at all, but for more senior trainees, their usefulness will vary. The realism they reproduce will always be secondary to that of the real-life clinical environment, and therefore ongoing validation studies are crucial to determine to what extent their use actually fulfills the learning requirements of trainees at different stages of training.<sup>26,27</sup>

In the authors' institution, they conducted a survey amongst trainees to explore in greater detail the challenges they face in their training. The points that the exercise raised were in congruence with the above arguments. One respondent argued that being part-time often results in them missing days when intervention is happening. Variance in difficulty between cases, lack of prior training, having different supervisors each time, and issues with patient's comfort during the procedure were also mentioned as challenges to training. Despite sessions taking place in a large teaching hospital, one trainee was concerned that the patient wasn't counselled properly, and worried that teaching might make the patient uneasy during the procedure. Trainees also agreed that available simulation models are not as good as practicing in a real-life environment. One urology trainee pointed out that at present there is

Table 1: Features of different simulation techniques for percutaneous nephrostomy.

Simulator type	Detailed pelvic/lyceal anatomy	Respiratory movements	USS puncture	X-ray guided	Contrast infusion	Haptic feedback	Progress tracking
Live animal	Yes	No	Yes	Yes	Yes	Yes	No
Biological bench top	Yes	No	Yes	Yes	Yes	Yes	No
Non-biological bench top	No	No	Yes	Yes	Yes	No	No
Virtual reality	Yes	Yes	No	Yes	Yes	Yes	Yes
Augmented reality	Yes	Yes	No	No	No	Yes	Yes
Cadaveric	No	No	Yes	Yes	Yes	No	No

USS: ultrasonography-snapshot.

neither a requirement by the Joint Committee on Surgical Training (JCST) nor formal training for UK urology trainees to gain any exposure to or competency in PCN. Finding time alongside their usual commitments poses another challenge. Any exposure in theatre to PCN and PCNL access is often ad hoc, and not formally recognised. This makes becoming proficient in ultrasound scanning and renal puncture challenging. Often, a radiology trainee will also be present at these lists, limiting the urology trainee's exposure.

In an era where all specialties are feeling the pressure of increased workload with limited resources, it can be argued that training urologists in PCN and percutaneous renal access would be of benefit. This would have the benefits of freeing-up radiology colleagues from attending urological theatre lists, and giving greater freedom to schedule urological cases requiring PCN access without affecting radiology commitments. This is a common problem at the authors' institution, where PCNL and antegrade procedures can only be performed on 1 day of the working week.

## RECOMMENDATIONS

PCN training involves facing a steep learning curve, and researchers have argued that a resident has to perform approximately 24 procedures in order to be proficient.<sup>27,28</sup> In their review of literature on training in percutaneous nephrolithotomy, Mishra et al.<sup>20</sup> described several categories where recommendations can be made in order to optimise training. They argued that before any formal training takes place, cognitive learning needs should be addressed, as most errors made by trainees in simulation usually result from their knowledge gaps rather than technical mistakes. They stressed the importance of a suitable, realistic, and risk-free training environment for the initial steps before practicing on patients, and recognised the usefulness of simulators for practice of repetitive tasking. They also argued that the most efficient wet-lab model is a live anaesthetised porcine, which closely replicates the human organ. The authors believe that all of these recommendations apply to trainees learning how to perform nephrostomies.

It is widely recognised that the most crucial task on which the procedure success heavily depends

during nephrostomy tube insertion is the initial access. Training methods should emphasise this critical step. Establishing the correct depth of initial percutaneous needle insertion is widely recognised as the critical initial challenge. The 3-finger technique described by Shergill et al.<sup>29</sup> is an example of a safe, cheap, and easy to learn method that can be used in teaching.

Some challenges faced by trainees will be unique to each institution, and therefore close supervision, feedback provision, and evaluation of the effectiveness of the adopted methods will undoubtedly be key elements. Conducting a simple survey amongst trainees can be a very useful tool. In the authors' experience, trainees argued that sufficient training opportunities exist; however, they emphasised their preference to be taught directly on patients by consultants rather than on simulators during routine outpatient lists.

These results may in part be due to the limited access to other training modalities, such as benchtop models or simulators at the authors' institution, and raises the question of whether the availability of such *ex vivo* training tools would have impacted the results of their survey.

The methods described within this overview allow for the training of a greater number of trainees in a safe, risk-free environment where repeated practice can be performed to not only achieve competence, but also confidence, in an era where training prospects are limited by workforce pressures and limited training opportunities. Moreover, it highlights how medical education is ever-evolving, and traditional methods of training are being adapted with state-of-the-art technologies to provide a lifelike *in vivo* training experience without any clinical risk, albeit at a cost. The greater potential

that this overview highlights is how methods of training used in surgery can also be utilised in other specialities to train in practical skills, with the potential for collaborative training and working (for example, between urologists and interventional radiologists). In the future, this may lead to a greater number of clinicians equipped with the skillset to perform such procedures independently, and has the potential to therefore alleviate stresses on acute services, and make changes in the workforce.

## CONCLUSION

Learning how to perform PCN can seem like a daunting task for doctors in training. It is undoubtedly an iterative process. Good understanding of the procedure, and repetition of the newly acquired skill with the aid of simulation and phantom models with direct feedback, followed by practice in a supervised clinical setting, are the fundamentals of an effective learning process. The authors believe that there is a role for *ex vivo* training tools, which can not only increase early exposure to the steps of PCN in a safe, risk-free environment, but can be used to train greater numbers of trainees than *in vivo* cases can. This method of training may therefore help to increase the number of radiology and urology trainees trained in PCN by levelling out opportunities to perform PCN in a classroom setting, with the overall potential to help streamline the intraoperative process for endourological procedures, as well potentially alleviating the burden of the interventional radiologists on call. Formal guidelines for establishing proper training sites do not exist, and therefore success will frequently depend on goodwill of mentors.

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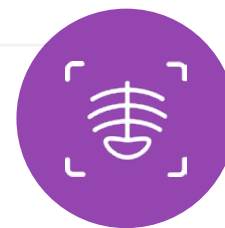
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# Migratory Loose Bodies from the Ankle Joint into the Flexor Hallucis Longus Tendon Sheath

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## Abstract

**Objective:** Loose bodies resulting from any form of osteochondral insult can migrate out of their intra-articular position to adjacent compartments. This retrospective study aims to illustrate the phenomenon of loose bodies migration from the ankle joint into the flexor hallucis longus (FHL) tendon sheath.

**Materials and Methods:** Cases of loose bodies in the FHL tendon sheath were identified from the authors' radiological database by way of keyword interrogation, covering the modalities of CT, MRI, and ultrasound over a period of 11 years. The imaging features of the loose bodies were recorded, together with the presence of ankle instability and osteoarthritis. Patient demographics and relevant history, including trauma and surgery, were collected.

**Results:** Thirty-four cases including 33 patients, with a total of 125 loose bodies in the FHL tendon sheath, were identified. There were 58 loose bodies (46.4%) in Zone 1 of the FHL tendon sheath, 65 loose bodies (52%) in Zone 2, and 2 loose bodies (1.6%) in Zone 3. All patients had features of ankle osteoarthritis on imaging, 14 of which had imaging features of ankle instability, and 19 patients had previous ankle trauma.

**Conclusion:** Osteochondral loose bodies originating from the ankle joint can migrate into the FHL tendon sheath. It is important to recognise this phenomenon as a distinct entity, different from primary tenosynovial chondromatosis of the FHL tendon sheath, which may have a different surgical management and clinical outcome. Detection of FHL tendon sheath loose bodies should also prompt closer examination for articular disease in the ankle joint.

## Key Points

1. Loose bodies resulting from any form of osteochondral insult, including osteoarthritis, trauma, neuropathic arthropathy, and inflammation, can migrate out of their intra-articular position to adjacent compartments.
2. This case series found 34 cases with 125 loose bodies having migrated from the ankle joint into the flexor hallucis longus (FHL) tendon sheath, identified via MRI, CT, or ultrasound.
3. It is important to recognise migratory loose bodies in the FHL tendon sheath as a distinct entity from primary tenosynovial chondromatosis as this may influence surgical management and clinical outcome.

## INTRODUCTION

Communication between the flexor hallucis longus (FHL) tendon sheath and the ankle joint is well-recognised and is reportedly present in around 17% of individuals.<sup>1</sup> However, migration of osteochondral loose bodies from the ankle joint into the FHL tendon sheath is not a well-recognised phenomenon, with only one case described in the radiology literature so far.<sup>2</sup> The authors hypothesise that loose bodies in the FHL tendon sheath migrated from the ankle joint, and the authors conducted this study to show their origin.

## MATERIALS AND METHODS

Cases of loose bodies in the FHL tendon sheath were identified from the authors' radiological database by interrogating the body of reports for the keywords of "loose body" or "loose bodies" and "flexor hallucis longus" or "FHL." The period of the past 11 years was queried, covering the modalities of CT, MRI, and ultrasound.

The reports were scrutinised to only identify the cases that specifically documented the presence of loose bodies in the FHL tendon sheath. All cases then had their relevant imaging reviewed by two musculoskeletal radiologists (1 year and 40 years' experience) in order to document the number, size (largest dimension), location, and imaging appearances of the loose bodies.

The locations of the loose bodies were grouped into Zone 1 (behind the ankle joint to the orifice underneath the sustentaculum tali), Zone 2 (from the tunnel underneath the sustentaculum tali to the knot of Henry), or Zone 3 (a segment of

FHL distal to the master knot of Henry to the phalangeal insertion).<sup>3</sup> In addition, to differentiate from intratendinous calcification, the loose bodies had to be surrounded by tenosynovial fluid or be seen to efface the edge of the tendon or myotendinous junction of the FHL to be considered eligible. Cases with CT images were also assessed in multiplanar reconstruction to confirm their location within the tendon sheath if required. Cases with ultrasound examination had to demonstrate, on the saved static images, the loose bodies surrounded by anechoic fluid adjacent to the FHL tendon. Presence of radiological evidence of osteoarthritis and instability (asymmetric joint space loss and increased tibiotalar tilt) of the ankle joint were also recorded. Clinical notes were assessed to check for any previous history of trauma or surgery to the ankle joint.

CT images had been acquired on Siemens 16-slice or 64-slice scanners. MRI images had been acquired on a Siemens 1.5T or 3T scanners (T1 sagittal, T1 turbo inversion recovery magnitude sagittal, proton density with fat saturation [PD FS] coronal, PD FS axial). If a magnetic resonance (MR) arthrogram was performed, the sequences obtained were T1 sagittal, T1 FS coronal, T1 FS axial, PD FS coronal, and PD FS axial. Ultrasound was performed using the ACUSON S2000 (Siemens Healthineers, Erlangen, Germany) system. This is a retrospective study and ethical approval was therefore not required.

## RESULTS

Initial interrogation of the authors' radiological database returned 127 cases that met the

keyword-search criteria. After manually going through the body of the reports, 36 cases were identified whereby loose bodies had been documented within the FHL tendon sheath at the time of reporting. The images were reviewed, and 2 cases were removed due to inability to adequately confirm the location of the loose bodies on CT and ultrasound respectively.

In the series of 34 cases (33 patients), the mean age of the patients was 56.9 years (range: 20–84). There were 8 female and 25 male patients. Thirteen of the cases were of the left ankle and 21 of the right ankle. In terms of modalities, there were 21 cases of loose bodies identified on MRI, 11 cases on CT, and 2 cases on ultrasound. Of the 21 cases of MRI, there were 3 cases of MR arthrography examination confirming the communication between the ankle joint and FHL tendon sheath. There were 2 further cases where there were large ankle effusion showing definite communication with the FHL tendon sheath.

There were, altogether, 125 loose bodies documented in the 34 cases. There were 58 Zone 1 loose bodies (mean: 6.1 mm; median: 5.0 mm; range: 1.0–20.0 mm), 65 Zone 2 loose bodies (mean: 5.0 mm; median: 4.0 mm; range: 1.0–13.0 mm), and 2 loose bodies in Zone 3 (mean: 3.5 mm; median: 3.5 mm; range: 3.0–4.0 mm). There were 16 cases of loose bodies in only Zone 1, 11 cases of only Zone 2, and 6 cases with loose bodies in both Zones 1 and 2. There was 1 case with loose bodies in all 3 Zones. Concurrent loose bodies in the ankle joints were also demonstrated in 21 patients.

All patients had radiographic features of ankle osteoarthritis, including 4 patients who already had ankle fusion or replacement, and a further 13 patients who subsequently underwent ankle fusion or replacement. There was radiographic evidence of ankle instability in 14 cases with asymmetric joint space loss and increased tibiotalar tilt, indicative of lateral ligament dysfunction. Nineteen cases had previous injuries, ranging from minor sprain to previous ankle fractures, including a patient who had previously had a microfracture for a large subchondral cyst following an osteochondral injury 8 years earlier. There were no cases of rheumatoid arthritis or septic arthritis. There was 1 patient with a history of diabetes, although

no features of diabetic neuropathy. Review of clinical notes revealed that the patients' main presenting complaints were related to their ankle joints rather than specifically from these loose bodies. There were no occasions where loose bodies in the FHL tendon sheath were detected on clinical examination.

## DISCUSSION

Intra-articular loose bodies can result as sequelae of a wide range of pathologies, including osteoarthritis, trauma, neuropathic arthropathy, and inflammation. Primary synovial chondromatosis is much rarer in comparison. Loose bodies can migrate out of their intra-articular location to adjacent compartments via naturally occurring communications. Whilst the authors' series had not radiologically demonstrated actual migration of loose bodies from the ankle joint with sequential or interval imaging, the majority of patients (61.8%) had loose bodies in both the ankle joint and the FHL tendon sheath. Furthermore, migration between these two compartments has been reported in the literature.<sup>2</sup> In addition, loose body migration between different compartments is well documented in other body areas, including the knee joint with popliteal cyst, hip joint with iliopsoas bursa, and glenohumeral joint with biceps tendon sheath.<sup>4–6</sup> Synovial chondromatosis of the subacromial bursa causing rotator cuff tear has also been reported, allowing the loose bodies to migrate into the glenohumeral joint.<sup>7</sup>

The authors grouped the location of the FHL tendon sheath loose bodies into Zones 1, 2, and 3 as per Lui<sup>3</sup> (Figure 1). This is clinically relevant should surgical intervention be considered, as these loose bodies have been reported to become symptomatic during weight-bearing.<sup>2</sup> Zone 1 tendoscopy is performed via posteromedial and posterolateral portals; Zone 2 is examined through posteromedial and plantar portals; and Zone 3 is examined through plantar toe portals.<sup>3</sup>

All patients in this study had radiological evidence of osteoarthritic changes in their ankle joint. Of note, a large proportion of patients (17/34 cases; 50%) either progressed to, or already had surgical fusion or replacement of

**Figure 1:** A 51-year-old male with ankle stiffness, swelling, and previous ankle sprain, requiring immobilisation in plaster 10 years previously.



A), B) and C) show CTs of the right ankle, demonstrating loose bodies (arrows) in Zones 1, 2, and 3, respectively.

their ankle joints. Nineteen of the cases also had suffered traumatic injuries to their ankles in the past. The authors believe these loose bodies have formed in the ankle joints from their osteoarthritis or trauma, which subsequently migrated into the FHL tendon sheath.

Interval imaging, where available, has also been reviewed. This revealed a few possible outcomes for the loose bodies. Firstly, the loose bodies may gradually change from a trabeculated to lucent appearance whilst maintaining a sclerotic rim. This is in keeping with fatty marrow replacement, reflecting maturation. This change is often accompanied by an increase in size (Figure 2). Secondly, loose bodies can also increase in size whilst maintaining their trabeculated pattern, with the maximal growth of 4 mm measured in a patient (most proximal loose body; Figure 3). Third and finally, the loose bodies can demonstrate gradual reduction in sizes and radiodensities (Figure 4), suggesting gradual resorption. Resorption of a loose body is only possible with synovial attachment to allow intra-synovial resorption.<sup>8</sup>

Synovial attachment would explain the relative static appearances of the loose bodies in

this patient despite them becoming smaller, which theoretically should have increased their propensity to become more mobile and relocate along the length of the whole tendon sheath. The presence of revascularisation, a requirement for ossification,<sup>9</sup> also provides another explanation as to why these loose bodies had remained not only in the same Zones, but roughly in the same position. In addition, just as myositis ossificans can resolve due to mechanical motion from muscle activity, the authors think loose bodies in the tendon sheath can also resolve via the same mechanism due to motion from the adjacent tendon.

The MR appearances of intra-articular loose bodies have been well-described in the literature<sup>10,11</sup> and can have variable signal, depending on the fat content and degree of calcification, differing between chondral, osteochondral, and osseous loose bodies. In the authors' series, 88 loose bodies were imaged on MRI; 24 demonstrated fatty marrow signal of high T1, low on fat-suppressed fluid sensitive sequences; 63 demonstrated low signal on both T1 and fat-suppressed fluid sensitive sequences; while 1 loose body had low T1 and intermediate to low signal on fat-suppressed, fluid-sensitive



Figure 2: A 60-year-old female with increasing ankle pain.



A) and B): lateral radiographs taken 24 months apart, showing initial dense appearance of two overlapping loose bodies (arrow and arrowhead) in image A), which altered to a radiolucent appearance with a sclerotic rim in B). Note slight increase in size. C) T1 sagittal and D) T1 TIRM are sagittal images demonstrating the larger loose body to have high marrow fat content.

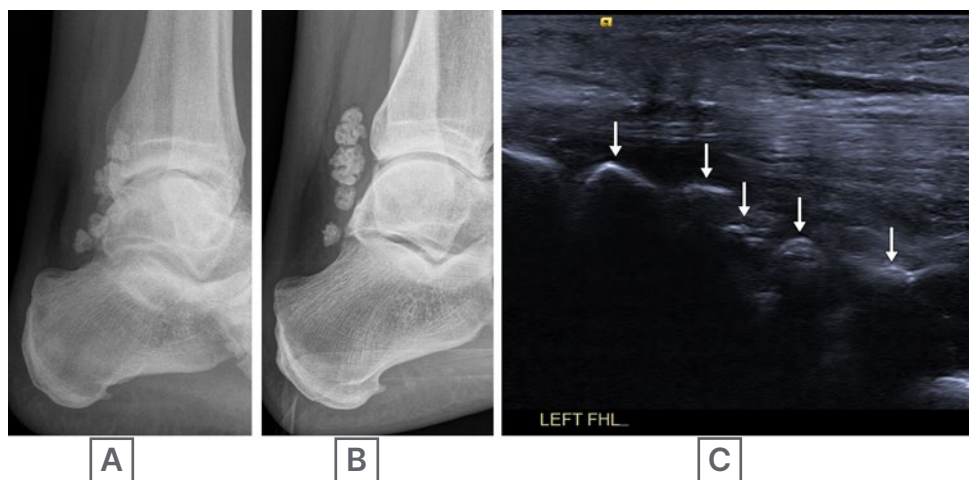
TIRM: turbo inversion recovery magnitude.

sequences (but non-ossified on CT), in keeping with a cartilaginous loose body.

There is a tendency for larger loose bodies to be seen in Zone 1 rather than Zone 2, in line with Lui's observations.<sup>12</sup> In the authors' series, 41.4% of Zone 1 loose bodies measured 8 mm or more compared with just 15.4% of Zone 2 loose bodies. The authors suspect that larger

loose bodies would be prevented from distal migration due to the limiting space in the tendon sheath. Some of the larger Zone 2 loose bodies were also noted to be aligned longitudinally with their largest dimension along the length of the FHL tendon sheath. The authors postulate that these loose bodies were of smaller sizes when they first migrated into Zone 2, where they subsequently grew in size with maximal growth

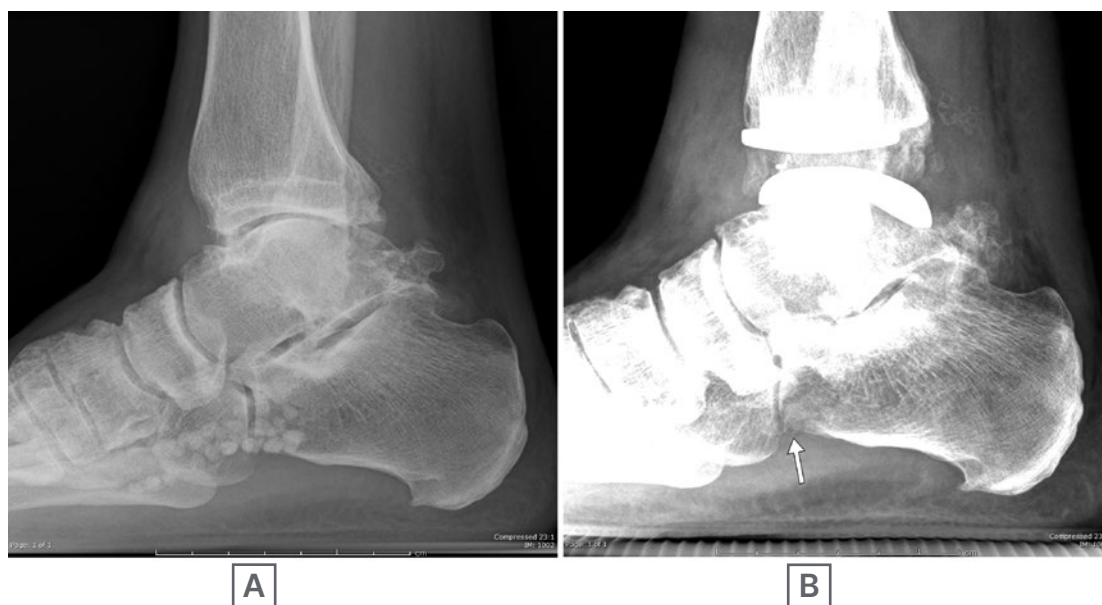
**Figure 3: A 47-year-old male with peroneal brevis tenosynovitis associated with a large ganglion (not shown).**



A) and B): lateral radiographs taken 41 months apart demonstrating multiple ossified loose bodies in Zone 1 of the FHL tendon sheath. These can also be seen on ultrasound (arrows) in image C), which is a longitudinal image across Zone 1 of the FHL tendon. The patient was asymptomatic from these loose bodies.

FHL: flexor hallucis longus.

**Figure 4: A 65-year-old male with progressive right ankle pain, limiting his activities.**



There are multiple loose bodies in the FHL tendon sheath, confirmed on MRI (not shown). A) and B) are serial radiographs of the right ankle, demonstrating severe ankle osteoarthritis in A), progressing later to ankle replacement. B) Multiple of the Zone 2 loose bodies have been resorbed 6 months after ankle replacement, with a few remaining visualised as centrally lucent, peripherally sclerotic loose bodies (arrow).

FHL: flexor hallucis longus.

along the longitudinal length of the FHL tendon sheath. In other words, the authors think the FHL tendon sheath may have influenced their growth to the longitudinal dimension.

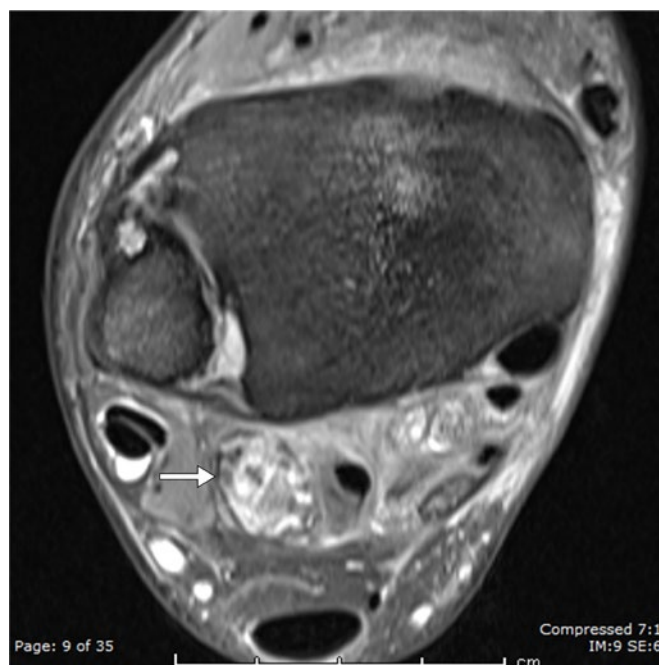
As far as the authors' know, there has only been one reported case of migratory loose bodies into the FHL tendon sheath.<sup>2</sup> It is important to distinguish this entity from other differential diagnoses such as primary tenosynovial chondromatosis of the tendon sheath where the ankle joint is normal<sup>12,13</sup> or myositis ossificans, where the ossification is intramuscular rather than in the tendon sheath.<sup>14</sup> Primary chondromatosis is conventionally described as a metaplastic process, though a cytogenetic study has proposed it to be a neoplastic process with chondral proliferation of the synovium;<sup>15</sup> it has a rare potential for malignant transformation.<sup>16</sup> Its aetiology is distinctly different from secondary chondromatosis, which is a sequela of osteochondral injuries. Furthermore, an important facet in the management of loose bodies, in general, is to determine and treat their underlying source;

this is equally if not more important than just surgically removing the loose bodies.<sup>17</sup> It is, therefore, important to appreciate this migration phenomenon so as not to overlook an ankle pathology such as advanced osteoarthritis.<sup>18</sup>

Determining the exact location of a loose body, whether it lies in the posterior recess of the ankle joint or in the FHL tendon sheath, can be difficult. This distinction is important<sup>12</sup> as access to the FHL tendon sheath loose bodies will require the endoscopist to surgically release the covering fascia.<sup>18</sup>

A loose body with high fatty content may be misdiagnosed as a lipomatous lesion on MRI, or even missed altogether on fat-suppressed or inversion recovery sequences (Figure 2). This can be prevented by correlating an MRI study with previous radiograph or CT examinations and, indeed, it should always be conducted when available. In addition, the authors found fat-suppressed sequences to be unhelpful, especially in the case of the spiculated loose body (Figure 5). However, interpretation of

**Figure 5: A 52-year-old male with progressive ankle pain, swelling, and osteoarthritis.**



PD FS axial image demonstrating a spiculated loose body (arrow), which is difficult to interpret in isolation without a plain radiograph or CT (performed, but not shown here).

PD FS: proton density with fat saturation.

the loose body is straightforward if correlated with either radiograph or CT. Nevertheless, MRI is superior in detecting non-mineralised loose bodies. Ultrasound can also be utilised to visualise loose bodies, revealing focal areas of high reflectivity with posterior acoustic shadowing indicating presence of peripheral mineralisation (Figure 3C). Cartilaginous loose bodies, on the other hand, may demonstrate hypoechogenic structures, with a central area of hyperechogenicity reflecting internal calcification.<sup>19</sup> Understandably, detection of loose bodies using ultrasound is aided by the presence of surrounding fluid.<sup>20</sup> The authors' experience has shown that ultrasound of these loose bodies can demonstrate a degree of limited mobility.

The authors' report constitutes the largest series of loose bodies in the FHL tendon sheath having migrated from the ankle joint to date. The strength of this study is that all their patients had either cross-sectional studies (CT or MRI) or an ultrasound examination, where the relationship of the loose bodies within the FHL tendon sheath can be determined with confidence. On MRI, the loose bodies must be surrounded by tenosynovial fluid, or be seen to efface the edge of the tendon or myotendinous junction. In addition, care was taken during review of CT to ensure it was not intra-tendinous calcification mimicking loose bodies in the tendon sheath; this is especially relevant in the context of previous trauma. In the presence of any ambiguity, the location of the calcification was assessed using multiplanar reconstruction. Indeed, as reported above, one case of CT has been removed due to inconclusive imaging appearance.

The authors noticed that there is a disproportionate high number of male patients (25 male and 8 female) and of the right ankle (21 right and 13 left) in their series. This can be partially explained by the fact that there were 6 male patients with football-related injuries. There were no female football-related injuries. In addition, right-footed dominance is more common in the general population.<sup>21</sup>

There are two weaknesses in this study. Firstly, the authors do not have histological data on the loose bodies, which would have been able to

definitively differentiate between primary and secondary synovial chondromatosis. A proportion of these patients had surgery to their ankle joints, but the FHL tendon sheath loose bodies had not been specifically addressed as they were not the cause of the patients' symptoms. Nevertheless, there are no imaging features supporting primary tenosynovial chondromatosis in this cohort. Tenosynovial chondromatosis lesions are either fusiform, round, or oval, and these features are not present in this cohort.<sup>22</sup> Furthermore, chondroid synovial proliferation, which is a recognised feature of primary synovial chondromatosis,<sup>23</sup> is not present in the authors' cases.

Secondly, the authors only have radiological confirmation of communication between ankle joint and FHL tendon sheath in five cases, by way of gadolinium confirmation or presence of large contiguous effusion on MRI. Literature has reported the presence of communication between the ankle joint and the FHL tendon sheath to be around 17%,<sup>1</sup> but it would have been ideal to confirm this communication radiologically by using, for example, iodinated contrast under fluoroscopy screening. However, this would have required an invasive procedure, which could not have been clinically justified.

## CONCLUSION

In summary, the authors' study represents the largest series showing loose bodies in the FHL tendon sheath having migrated from the ankle joint to date. Osteochondral insults in the ankle joint may produce loose bodies that can migrate into the FHL tendon sheath. All the patients in this study demonstrated osteoarthritis in their ankle joints, with a significant portion with advanced osteoarthritic changes and ankle instability. Presence of loose bodies in the ankle joint should prompt closer inspection of the ankle joint for any articular disease. Finally, it is important to recognise migratory loose bodies in the FHL tendon sheath as an entity distinctively different from primary tenosynovial chondromatosis as it may influence surgical management and clinical outcome.



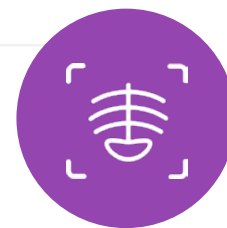
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# Facial Swelling as a Presenting Sign of Cholangiocarcinoma

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## Abstract

Cholangiocarcinoma is a rare primary malignancy of the biliary tree, which usually presents late in the course of disease with jaundice, upper right quadrant pain, and cachexia. They frequently metastasise in the lungs, liver, bones, adrenals, peritoneum, and retroperitoneal lymph nodes. The incidence of cutaneous dissemination from cholangiocarcinoma is extremely rare, with the scalp being the commonest distant site of skin metastasis. The authors report the case of a 44-year-old female with Stage IV hilar cholangiocarcinoma, who presented primarily with tender facial swelling, prompting investigation and subsequent diagnosis. To the authors' knowledge, this case is the first report of a cholangiocarcinoma presenting as facial metastasis. It highlights the need for early characterisation of cutaneous lesions, which are likely to be of neoplastic origin using histology, immunohistochemistry, and PET-CT scans, and reminds that biliary tree neoplasms are possible primary malignancies in cases of skin metastasis, especially in the head and neck region.

## Key Points

1. Cholangiocarcinoma is a rare primary malignancy of the intrahepatic or extrahepatic biliary tree, forming <2% of all primary cancers. Rarely, cholangiocarcinomas may present as isolated or multifocal cutaneous metastasis.
2. Cutaneous metastases arising from visceral malignancies are extremely rare, with overall incidence between 0.4% and 10.0%; of these, only 0.8% of cases present with cutaneous deposits as the first sign of malignancy.
3. Bile duct malignancy may be considered when addressing cutaneous metastasis of unknown origin, through histological and immunohistochemical analysis backed by clinical and radiological findings.

## INTRODUCTION

Cholangiocarcinoma is a malignancy of the intrahepatic or extrahepatic (perihilar or distal) biliary tree, forming less than 2% of all primary cancers.<sup>1,2,3</sup> They have a definite male preponderance, with peak incidence in the seventh decade of life.<sup>2</sup> Clinically, patients frequently present with jaundice, right hypochondriac pain, and weight loss. However, more often than not, the tumour is locally advanced or metastasised at detection, and patients miss the window for radical surgery,<sup>1,2</sup> which is the only potential curative treatment known.<sup>3</sup>

While the usual sites of spread from a primary cholangiocarcinoma are lungs, liver, bones, adrenals, peritoneum, and retroperitoneal lymph nodes,<sup>1,3</sup> the authors' survey of existing literature yielded a few reports of cholangiocarcinomas presenting as skin metastasis,<sup>1-6</sup> most of which already showed extensive visceral metastasis at diagnosis.<sup>6</sup> However, cholangiocarcinoma presenting as facial swelling is previously unreported.

## CASE REPORT

A 44-year-old female reported in February 2020 with a diffuse tender swelling over the right maxillary and zygomatic areas, of 45 days duration. It was associated with pain and watering from their right eye. There was no history of trauma, fever, pre-existing skin conditions, tuberculosis, or diabetes. Ultrasonography showed diffusely thickened hyperechoic subcutaneous lesion, with internal and peripheral vascularity on colour Doppler, raising suspicion of infectious or inflammatory aetiology.

A CT scan of the paranasal sinuses was performed due to clinical suspicion of invasive sinus pathology. This showed diffuse ill-defined soft tissue lesions in the subcutaneous and myofascial planes of the right premaxillary, prezygomatic, and frontal regions (Figure 1A-C). On MRI, the lesions had homogeneous T2-weighted (T2W)/short-tau inversion recovery hyperintense (Figure 1D-G) and T1-weighted (T1W) isointense signal characteristics relative to muscles (Figure 1H), with diffusion

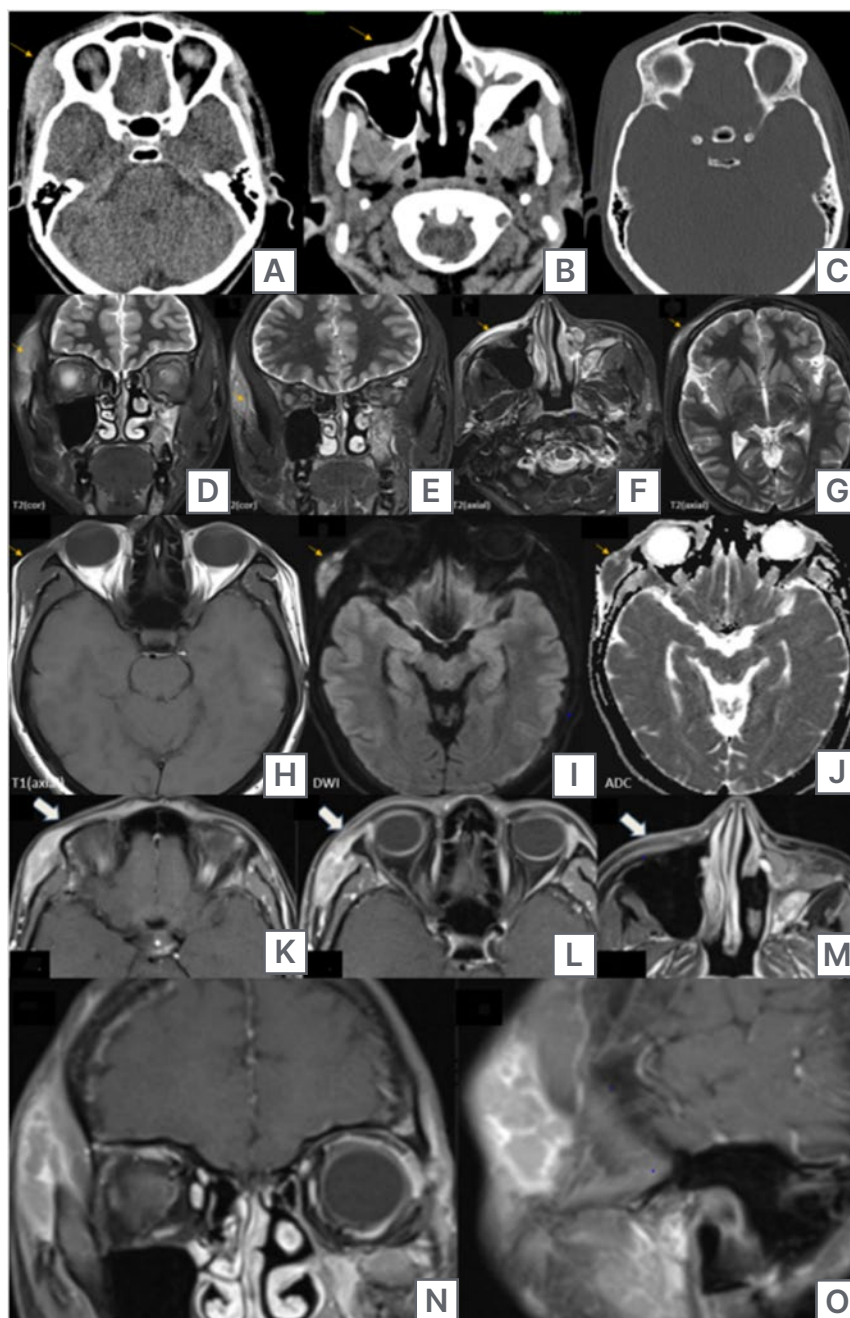
restriction (Figure 1I and J) and heterogeneous post-contrast enhancement (Figure 1K-O). These findings indicated a possible neoplastic infiltrative lesion. For confirmation and further management, the patient was advised biopsy correlation, which was refused, and the patient took discharge, against medical advice.

In May 2020, the patient returned with 7 days' history of jaundice, right hypochondriac pain, and another new soft tissue swelling over her right arm. The patient had no history of hepatotoxic drug intake or alcohol use. Hyperbilirubinaemia with increased liver enzymes was present. Viral markers for hepatitis were negative.

Ultrasonography of abdomen and pelvis, which was performed at another centre, showed asymmetric intrahepatic biliary radical dilatation in both lobes of the liver, due to a nearly isoechoic mass at the common hepatic duct bifurcation, which was marginally infiltrating into the cystic duct. The common bile duct (CBD) measured 10 mm in diameter. Multiple periportal lymph nodes were seen, the largest measuring around 16 mm.

A triple phase CT scan confirmed the presence of an infiltrative enhancing soft tissue density mass at the common hepatic duct bifurcation (Figure 2A-D), extending into proximal CBD and distal cystic duct, measuring about 39×32×31 mm (transverse x craniocaudal x anteroposterior). Upstream dilatation of the right and left hepatic ducts and intrahepatic biliary radical were noted. Periportal and retroperitoneal lymphadenopathy were present. Enlarged periportal lymph nodes were compressing the portal vein extrinsically. Right paraspinal soft tissue lesions were detected at the ninth and tenth thoracic vertebral levels, suspicious of metastatic deposits. Magnetic resonance cholangiopancreatography confirmed the findings of CT and ultrasonography. The mass had T1-W hypointense and T2-W hyperintense (Figure 2E and F) signal relative to liver, with restricted diffusion. Abrupt cut off of right hepatic duct was seen (Figure 2G and H). It terminated into an intraluminal soft tissue component measuring 7×3 mm in the mid-portion of CBD (Figure 2F), causing a meniscus sign (Figure 2H). Pancreatic portion of CBD was normal. The mass at porta hepatis was compressing the portal vein (Figure 2E) and

Figure 1: A CT scan of the paranasal sinuses



A) A CT scan of the paranasal sinuses showing ill-defined iso- to hyperdense lesion in the skin, subcutaneous, and myofascial planes and B) pre-maxillary regions. B) Incidentally detected, fibrous dysplasia of the left maxillary sinus. C) No bony erosion can be seen on the bone window.

D and E) T2 hyperintense infiltrative lesion in the right zygomaticotemporal, F) maxillary, and G) frontal soft tissues.

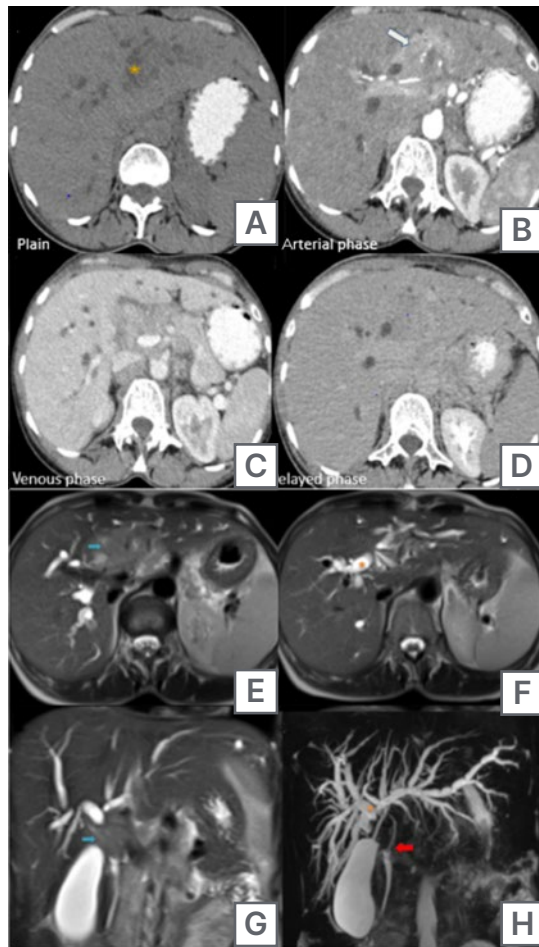
H) Lesions appear to be isointense to the muscle on T1-W, with I) diffusion restriction, and J) corresponding low ADC values.

K-O) Post-contrast MRI sequences show the heterogeneous enhancement of these lesions (the arrow), suggesting neoplastic cutaneous lesions.

ADC: apparent diffusion coefficient; T1-W: T1-weighted.



**Figure 2: A triple phase CT scan confirmed the presence of an infiltrative enhancing soft tissue density mass at the common hepatic duct bifurcation.**



A) A Contrast-enhanced CT scan of the abdomen showing an infiltrative soft tissue mass (star) at the bifurcation of CHD. B) It shows heterogeneous enhancement (arrow) in the arterial phase and related to the right and left hepatic ducts. C and D) The mass is hypoattenuating to the liver in venous and delayed phases. C) The common bile duct is compressed and not well visualised.

E and F) An MRCP showing a heterogeneous T2-W hyperintense mass at the CHD bifurcation (blue arrow). G and H) Abrupt cut-off (star) and non-visualisation of CHD by the mass, which is likely to involve the distal cystic duct. F) It is extending to the CBD, causing H) meniscus sign (red arrow). The rest of the distal is normal. E-H) Asymmetric upstream dilation of the right and left hepatic ducts and IHBR due to obstruction by the mass.

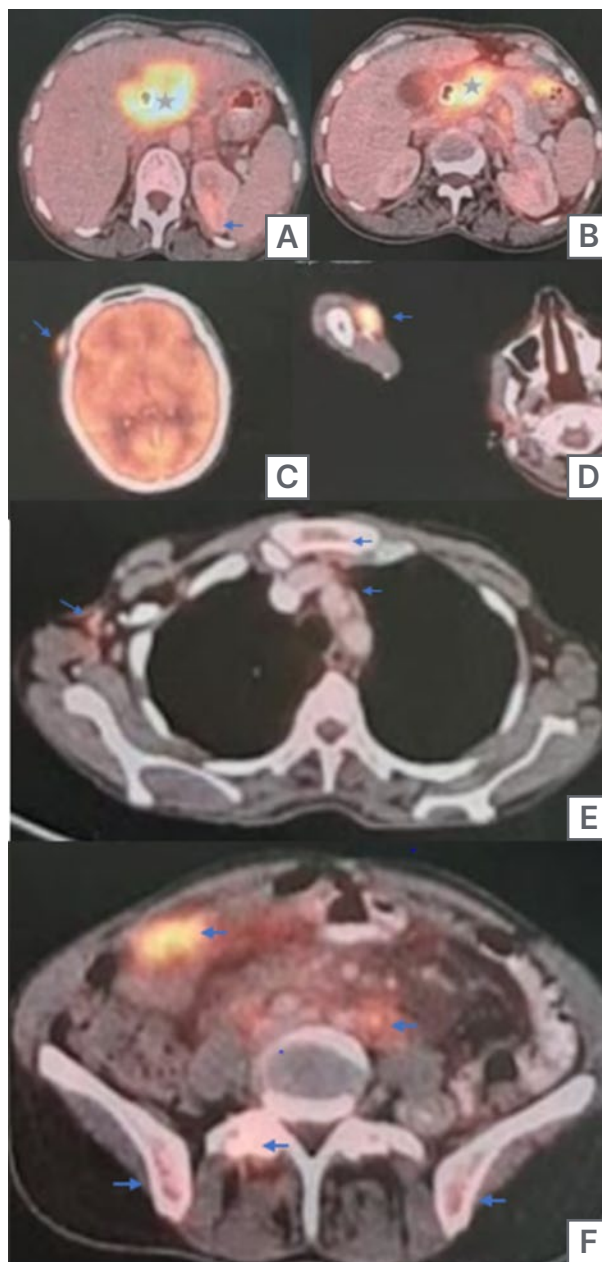
CBD: common bile duct; CHD: common hepatic duct; IHBR: intrahepatic biliary radicals; MRCP: magnetic resonance cholangiopancreatography; T2-W: T2-weighted.

distal cystic duct, which showed abrupt cut off (Figure 2F and H).

A biopsy of the mass showed central vein and portal triad, with inflammatory cells, suggesting triaditis. Dense fibrocollagenous stroma infiltrated by discrete tumour cells was observed. The tumour cells showed pleomorphic nuclei and

hyalinised collagen, with occasional ill-defined glandular differentiation with extracellular mucin. Hepatocytes showed cholestasis, focal steatosis, and regenerative changes. These findings were positive for poorly differentiated sclerosing cholangiocarcinoma.

Figure 3: A PET-CT detected fluorodeoxyglucose-avid visceral metastasis.



A) An FDF-PET-CT scan showing cholangiocarcinoma primary (star) at CHD bifurcation, encasing the right and involving the left hepatic ducts and B) CBD. A) Metastatic deposits (blue arrow), as shown, are left suprarenal metastasis.

C) FDG-avid cutaneous metastasis in the right frontal scalp and D) right arm.

E) Mediastinal, retrosternal, retroperitoneal, mesenteric, and F) pelvic nodal metastasis.

E) Skeletal metastasis in sternum, vertebrae, and F) iliac bones.

CBD: common bile duct; CHD: common hepatic duct; FDG: fluorodeoxyglucose.

A PET-CT performed in June 2020 detected fluorodeoxyglucose-avid visceral metastasis (Figure 3) in Segment II of the liver, left

suprarenal gland; nodal metastasis in left supraclavicular, retrosternal, mediastinal, right paravertebral, mesenteric, retroperitoneal, pelvic,

and bilateral inguinal regions; skeletal metastasis in cervical–thoracic–lumbar vertebrae, sacrum, bilateral pelvic bones, femurs, humeri, scapulae, ribs, and sternum; and subcutaneous or myofascial metastasis in frontal scalp, right frontotemporal region, right cheek, and both arms.

A final diagnosis of hilar cholangiocarcinoma, with first order right hepatic duct and second order left hepatic duct involvement, and hepatic parenchymal infiltration was reached:

Bismuth–Corlette classification Type IV. Regional and distant lymph nodal, hepatic, adrenal, skeletal, and cutaneous metastasis indicated Stage IVB cancer.

The patient underwent palliative extrahepatic biliary drainage, with placement of two metallic biliary stents, followed by four cycles of chemotherapy with folinic acid plus fluorouracil plus oxaliplatin, and is being maintained on oral capecitabine.

## DISCUSSION

Cutaneous metastases arising from visceral malignancies are extremely rare, with studies reporting variable overall incidence between 0.4–10.0%.<sup>2,3,7</sup> Amongst these, a mere 0.8% of cases presented with cutaneous deposits as the first sign of malignancy.<sup>6</sup> Excluding malignant melanoma and lymphoma, breast cancer (36.2%), followed by cancers of the lungs (16.3%), colorectal (11.3%), oral mucosa (7.8%), stomach (7.1%), liver (2.8%), oesophagus (2.1%), and kidney, ovary, prostate, and bladder (<1%) showed higher propensity to metastasise to the skin.<sup>3,7</sup> Overall, the chest, abdomen, and scalp were the predominant sites for metastasis.<sup>7</sup> This is theorised to be due to the dissemination of tumour cells via valveless vertebral venous plexus communicating segmentally with veins of thorax, abdomen, pelvis, and the intracranial dural sinuses.<sup>4</sup>

Clinically, cutaneous metastasis most commonly present as painless nodular lesions, although macules, plaques, ulcers, erythema,<sup>3</sup> scarring alopecia, cutaneous horns, and pyoderma gangrenosum-like lesions have also been described.<sup>7</sup>

Diagnosis of an occult primary tumour from a cutaneous metastasis is possible by histological and immunohistochemical analysis. Typically, tumour cells spare the epidermis, while infiltrating the dermis and subcutaneous tissues. Immunostaining of a metastatic deposit from bile duct malignancy will be cytokeratin-7 positive, cytokeratin-20 positive, or CDX2 negative.<sup>8</sup>

## CUTANEOUS METASTASIS IN CHOLANGIOCARCINOMA

Cholangiocarcinomas disseminate by seeding at the site of percutaneous biliary drainage over thorax (30.3%) or abdomen (20.0%) through catheter tracts, and by metastasising to distant sites, commonly scalp (12.6%), back, or thigh.<sup>1,6</sup> Liu et al.<sup>1</sup> systematically analysed reports of cholangiocarcinoma presenting with cutaneous metastasis from 1978 to 2014, which yielded only 30 cases from 21 studies. Amongst these, skin lesions were the first sign of the malignancy in 26.7% cases. The cases had a median age of 60 years at diagnosis and definite male predilection. Further, solitary cutaneous metastasis at diagnosis and male sex showed poor outcome. Median overall survival after cutaneous metastasis in cholangiocarcinoma was just 4 months.<sup>1</sup> The poor prognosis was likely as the majority of such cases already had extensive visceral metastasis (73.8%) at diagnosis.<sup>6</sup> These findings underscore the importance of early diagnosis of cholangiocarcinoma and the high degree of suspicion required when approaching suspicious skin lesions.

## CHALLENGES IN IMAGING OF CUTANEOUS METASTASIS

When imaging a cancerous-looking skin or soft tissue lesion, primary skin malignancies (e.g., squamous cell skin cancer, basal-cell carcinoma, melanoma, etc.) and lymphomas are the usual suspects, while metastasis is scarcely considered. Moreover, benign, premalignant, and infectious or inflammatory lesions may mimic a neoplasm, confounding diagnosis. Neoplastic cutaneous lesions may have been incidentally detected, or alternatively can be vague, even when they are the lesions of interest, when located at the edge of an image. Hence, multimodality imaging using CT scans, magnetic resonance studies and PET-

CT are useful for accurate diagnosis, staging, treatment planning, and assessment of therapeutic response. CT scans have the advantage of being widely available, cost-effective, and are able to detect pulmonary metastases. Meanwhile, anatomical resolution of superficial tissues provided by MRI is superior. PET-CT is most useful in detecting micrometastasis, indeterminate metastatic nodes, and subtle tumour recurrence.<sup>5</sup>

## CONCLUSION

Cholangiocarcinoma is a rare primary malignancy, which may rarely present as isolated or multifocal

cutaneous metastasis. Therefore, probability of bile-duct malignancy should also be kept in mind when addressing cutaneous metastasis of unknown origin. This can be done by histological and immunohistochemical analysis, backed by clinical and radiological findings.

This case of a 44-year-old female with Stage IVB hilar cholangiocarcinoma, first presenting with painful facial swelling, truly highlights the occult nature of bile duct malignancy, its variable presentation, and the clinical vigilance required for its diagnosis.

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