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EMJ Radiology

Review of ECR 2023

Editor's Pick

Utility of Bedside Lung Ultrasound in the Assessment of Volume Status in Patients on Chronic Haemodialysis

Interviews

Hear career insights from two key players at ECR 2023, ESR President Adrian Brady and EFRS President Andrew England

Contents

Editorial Board

Aims and Scope

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EMJ

Welcome letter

Evgenia Koutsouki
Editor

Dear Readers,

Welcome to the latest issue of *EMJ Radiology*, covering highlights from the European Congress of Radiology (ECR) 2023. It was an absolute delight for the EMJ team to attend the congress in person and hear the amazing research and new studies in the field first-hand. With the theme of the congress being 'The Cycle of Life', signifying the role of radiology at different stages of life, the opening ceremony was nothing short of spectacular, with a video reel to put the theme in context, as well as a live orchestra. The conversations this year were very much dominated by artificial intelligence, and how this is rapidly changing the field.

In this issue, we have brought some of the key highlights of the congress by summarising the session on breast imaging at different phases of life, which was in line with the theme of the congress. We are delighted to feature interviews with the European Society of Radiology (ESR) President Adrian Brady, and Andrew England, President of the European Federation of Radiographer Societies (EFRS). Our issue would not be complete without our array of peer-reviewed articles covering a plethora of topics in the field.

This issue has come together thanks to the amazing contribution of our authors, interviewees, and peer reviewers, so I would like to thank everyone who has helped in the publication of this content. With their amazing expertise and key insights, the members of our Editorial Board have helped to elevate the quality of this content. I hope you enjoy reading this issue, and I look forward to next year's ECR.

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Foreword

Dear Colleagues,

Welcome to the most recent issue of *EMJ Radiology*. Here we explore content featured at the European Congress of Radiology (ECR) 2023, which returned this year both on-site in the beautiful city of Vienna, Austria, and digitally for those who could not make it in person. This issue of *EMJ Radiology* brings together a range of content from radiologists all over the world.

Included are interviews from representatives of the European Society of Radiology (ESR), including Andrew England, European Federation of Radiographer Societies (EFRS) President, and Adrian Brady, ECR President. These esteemed colleagues share their in-depth knowledge of the ESR, focusing on the value of the society and this year's ECR congress. This edition also features an interview from Katherine Andriole, Associate Professor of Radiology, Brigham and Women's Hospital, Harvard Medical School, and Director of Academic Research and Education Mass General Brigham (MGB) Data Science Office, Boston, Massachusetts, USA, who discusses her illustrious career and her work on picture archiving and communication systems.

This edition also features novel articles from authors in the field. Bhardwaj et al.'s insightful study evaluates the use of lung ultrasound as a non-invasive adjunct to physical examination in patients with end-stage renal disease. El Hussini et al. explore the correlation between chest legions in CT, neutrophil-lymphocyte ratio, and platelets-lymphocyte ratio in patients with COVID-19 for their value as an early warning sign of severe COVID-19.

Featured alongside these fascinating articles is a review of findings from the ECR 2023 Congress. This review includes late-breaking research abstracts, fascinating features covering key sessions, and insightful interviews with key individuals within the congress.

I would like to thank all of those who have contributed to this fantastic issue of *EMJ Radiology*, and I hope that you enjoy reading this journal.

Yasmeen Malik
St. George's, University of London, UK

ECR 2023

Review of the European Congress of Radiology (ECR) 2023

Location:	Vienna, Austria, and online
Date:	1st–5th March 2023
Citation:	EMJ Radiol. 2023; DOI/10.33590/emjradiol/10301730. https://doi.org/10.33590/emjradiol/10301730.

THIS YEAR, the European Society of Radiology (ESR) welcomed 17,262 participants from 122 different countries to their congress in Vienna, Austria, and online. After the online congresses in 2020 and 2021 due to COVID-19, and the congresses both in-person and online last year, ESR president Adrian Brady introduced this year's congress as a tribute to the past presidents who dedicated themselves to achieving success in difficult times.

After a few disruptive years, during which the ESR had to show their innovation and willingness to change in order to ensure that their mandates and responsibilities were still fulfilled, the ESR has tried their best to create a safe environment in which the standard of professional and educational content remains high. Brady began the opening ceremony by thanking everyone who dedicated their time to making this congress a success, including all those involved in planning the congress, but also all ESR members.

Brady then introduced the theme for this congress, 'The Cycle of Life'. This theme aimed to bring attention to the importance of the role of radiology and radiography at all stages of life, from before it begins until after it ends. Numerous sessions throughout the programme were given this tag, so that participants could easily spot those sessions that covered a specific stage in life, or unusual applications of techniques. This theme allowed for a programme filled with unusual topics such as forensic imaging; the use of imaging in palaeontology and archaeology; the investigation of artworks and musical instruments; and the use of radiology in the generally healthy, for example through sport applications.

> **"Technical innovation, if embraced in the right way at the right time, can lead to huge leaps in human endeavour."**

As is tradition, ESR chose one 'in focus' group to be given particular attention at the congress: trainees. While the congress featured materials suited for practitioners at any stage of their career, the ESR added emphasis to areas that would interest trainees, including work-life balance, career development, mentoring, diversity, and equality and inclusivity.

At the opening ceremony Brady gave advice to the trainees in the audience, starting with the importance of accepting imperfection and trying to learn and strive to be the best you can be, while being kind to yourself and your colleagues when you or they fail after having tried diligently. Brady highlighted that radiology is a rapidly changing specialty, explaining that much of what is taught today will be redundant by the time practitioners reach the middle or end of their career. Brady stressed the importance of innovation in this change, saying: "Technical innovation, if embraced in the right way at the right time, can lead to huge leaps in human

endeavour." Finally, Brady reminded trainees to be aware of changes. The COVID-19 pandemic has created distance between radiologists and their patients and referrers. Brady encouraged trainees and their seniors to show others the importance of their role, and to make themselves indispensable to secure the future of radiology.

At the opening ceremony, six awards were granted in recognition of outstanding, internationally-recognised achievements and leadership. First, ESR honorary membership was granted to Beatriz González Ulloa, Dei Diagnóstico Especializado Por Imágen, Zapopan, Mexico, for their work in the field of breast imaging; Bruce G. Haffty, Rutgers Cancer Institute of New Jersey, New Brunswick, USA, for their work in radiation oncology; and finally, James Griffith, The Chinese University of Hong Kong (CUHK), for their work in the field of musculoskeletal imaging. Three gold medals were also awarded to Sue Barter, Addenbrooke's Hospital, Cambridge, UK, for their work in breast and gynaecological imaging and in clinical audit and governance; Christoph D. Becker, University of Geneva, Switzerland, for their work in abdominal, diagnostic, and interventional radiology; and Lorenzo Derchi, University of Genoa, Italy.

The EMJ team was delighted to be a part of this congress, and is looking forward to ECR 2024, which will take place in Vienna from 28th February–3rd March. Read on for this year's scientific highlights, covering topics such as saving energy in radiology departments and magnetic resonance-planimetry in multiple sclerosis, as well as interviews with ESR president Adrian Brady, and European Federation of Radiographer Societies (EFRS) president Andrew England.

"This theme aimed to bring attention to the importance of the role of radiology and radiography at all stages of life, from before it begins until after it ends."

Artifical Intelligence: Tacking Dataset Deficiencies in Brain Metastases

RESEARCH investigating the merit of medical artificial intelligence (AI) has previously suggested that AI is of little use in clinical practice due to poor quality datasets. The Stanford BrainMetShare Dataset, the only available dataset for brain metastases, is limited to 156 cases, focusing on just six primary tumour types. Work published attempting to predict tumours from MRI again only focuses on six of the most common primary tumour types. Thus, these datasets are inadequate as "many of the rare cases are regularly neglected," noted Quirin Strotzer, Department of Radiology, University Hospital Regensburg, and Department of Neuroradiology, Medbo District Hospital Regensburg, Germany, who called for higher quality, diverse datasets in medical AI during their presentation at ECR 2023.

Strotzer and colleagues recruited patients between 2003–2021 with cerebral metastases who had tumour histology and pre-therapeutic MRI data (T1, T1CE, T2, fluid-attenuated inversion recovery) available. Data from 3D T1 post-contrast magnetisation prepared-rapid gradient echoes were also utilised where possible (87.6% of patients). Clinical parameters were recorded for each patient, including gender, age, Eastern Cooperative Oncology Group (ECOG) performance status, BMI, histology, survival, extracerebral metastases, and therapy. MRI data was then collected, and a bias correction was applied before co-registering the different images and applying an intensity normalisation. Based on a U-Net trained on brain tumour segmentation (BraTS) data, three different segment labels were then applied and manually verified: oedema, non-enhancing tumour, and enhancing tumour.

"Strotzer and colleagues generated a standardised, multisite, multi-vendor dataset of pre-operative MRIs of brain metastases."

The final dataset contained 231 patients with 647 metastases. Fifteen different MRI scanners generated images, with the vast majority originating from 1.5T scans (89%). Unlike previous datasets, 27 primary tumour types were included, highlighting that the metastases most frequently originated from lung adenocarcinoma (181 cases), followed by melanoma (119) and breast cancer (85).

To conclude, Strotzer and colleagues generated a standardised, multisite, multi-vendor dataset of pre-operative MRIs of brain metastases. They described it as the largest, most heterogenous dataset available, with higher accuracy to medical reality. In future, they believe the dataset could be easily expanded to incorporate DNA mutation data.

Mammography Screening Using Artificial Intelligence

RETROSPECTIVE results from a mammography screening study were presented at the ECR 2023, held in Vienna, Austria, in March 2023. The aim of the Section for Breast Cancer Screening at the Cancer Registry of Norway was to compare rates of cancer detection using two CE-marked artificial intelligence (AI) systems, using the same retrospective data set.

Breast cancer is the most common cancer for females in Norway, and 3,991 females were diagnosed with the disease in 2021. In the country, females between the ages of 50 and 69 are invited for a screening mammogram at 2-year intervals, with the aim of finding early-stage breast cancer, and preventing unnecessary deaths from the disease. All breast screens in Norway are independently interpreted by two radiologists who specialise in breast imaging.

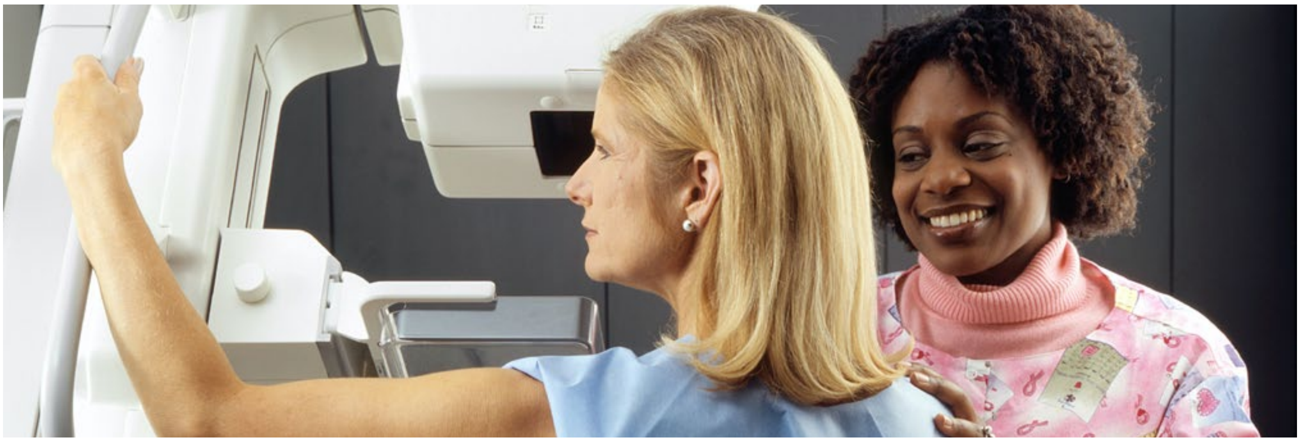
In total, the study analysed 106,380 examinations, which were carried out between 2009–2019 in the county of Østfold in southeastern Norway. The data set was provided by BreastScreen Norway, part of the Cancer Registry of Norway, and the study used images taken by Siemens MAMMOMAT Inspiration (Munich, Germany).

Measures were interpreted by two AI systems: A and B. During this process, 645 screen-detected cancers and 173 interval cancers were found. System A selected 91% (587 out of 645) of screen-detected cancers and 43% (74 out of 173) of interval cancers, and System B selected 84% (540 out of 645) of screen-detected cancers, and 37% (64 out of 173) of interval cancers, respectively. A and B agreed in 53% of examinations selected in this study. Researchers found that 93% of screen-detected cancers and 50% of interval cancers were selected by systems A or B.

Solveig Hofvind, Section for Breast Cancer Screening, Cancer Registry of Norway, Oslo, Norway, pointed out that the limitations of the study are that it was carried out at a single centre; it is unknown whether the location detected by AI represents the real location of the cancer; and the differentiation between missed versus true interval cancers.

In future, Hofvind added, the analysis of the study will be extended to include more centres across all of Norway's regions. Researchers also want to look into the possible benefits of using two or more AI systems working concurrently, and the use of AI as a support in screen-reading, or to triage screen examinations. Any future prospective studies will be based on this analysis, which was carried out using retrospective data. ●

"In total, the study analysed 106,380 examinations, which were carried out between 2009–2019 in the county of Østfold in southeastern Norway."



No Time to Be Idle in Radiology Departments

RADIOLOGY departments consume large amounts of energy, with a single CT scanner having the energy consumption of five four-person households. Over two-thirds of this energy is used when in an idle state, according to Manfred Tobias Meyer, Department of Radiology and Nuclear Medicine, University Hospital Basel, Switzerland, who presented these findings at ECR 2023.

Meyer and colleagues monitored approximately 60 medical imaging systems, including five CT, six MRI, two PET-CT, 12 radiography units, four angiography units, and seven ultrasound machines, as well as 80 picture archiving and communication system workstations, 165 personal computers (PC), six smart monitors/PCs, and 53 printers in their department. They were able to determine the devices' online status by internet control message protocol echoes, requested in 15-minute intervals, which were presented on live dashboards.

The devices were tracked for 2 weeks in October and November 2022. Then, the project was announced in mid-November to raise awareness. They continued to track device usage to analyse changes in behaviour, and identified constantly running modalities that could be turned off.

There was a reduction in the number of devices left on during off hours. For example, the two PET-CT scanners are now being turned off over the weekend and overnight. In the next 4 months, one scanner saved 2,366 kW/hour of energy, equivalent to 520.53 CHF and 302.85 kg of carbon dioxide emissions. The projected savings are 72,337.3 kW/year, equivalent to 19,530.90 USD and 9,259.0 kg of carbon dioxide.

However, there were limitations in this study, as devices with no network connection (e.g., most monitors) could not be tracked, and printers could not be reliably tracked because the network status remains on while in standby.

Despite this, idle devices present a significant opportunity to save on costs and energy, and raising awareness had a quantifiable effect on the turn-off rates of PCs, with estimated yearly savings in Meyer's department of 13.9 four-person households.

"In the next 4 months, one scanner saved 2,366 kW/hour of energy, equivalent to 520.53 CHF and 302.85 kg of carbon dioxide emissions."

Magnetic Resonance Texture Analysis for Assessing Bowel Wall Fibrosis

CROHN'S disease (CD), a chronic inflammation of the gastrointestinal tract, affecting 1.5 million people in Europe. The detection of fibrotic strictures to assess therapeutic management for CD is a major challenge. Inflammatory strictures require medical therapy, whereas fibrotic strictures require surgical treatment. Histopathology is the gold standard for stricture diagnosis, but MRI represents an important technique to assess disease activity, and for first diagnosis.

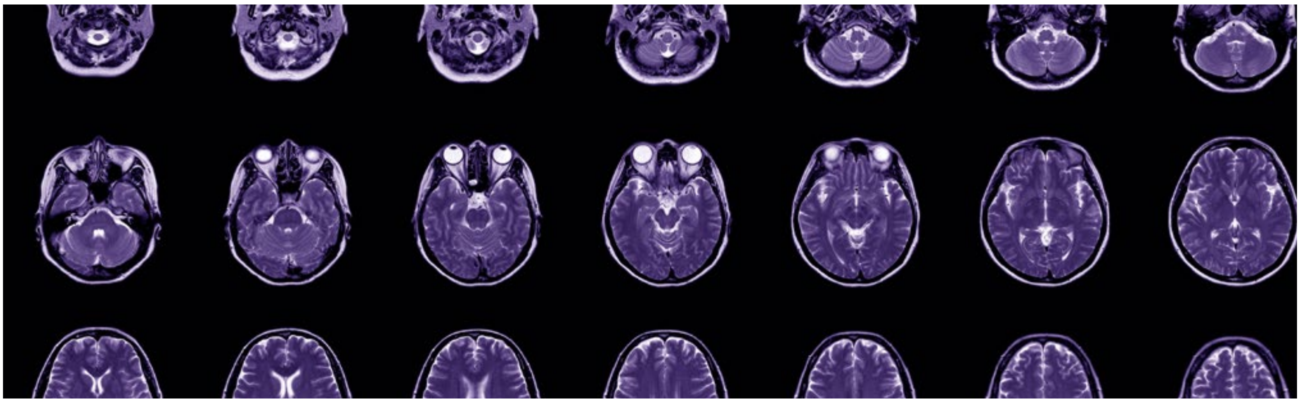
At ECR 2023, lead author Chiara Zanon, Department of Medicine-DIMED, Institute of Radiology, University of Padua, Italy, presented the results of a retrospective observational study conducted between January 2012–December 2020. Researchers aimed to investigate whether texture analysis of magnetic resonance enterography could detect intestinal fibrosis in patients with CD. All patients (n=35) had no magnetic resonance artifacts, had undergone elective bowel resection, and had an magnetic resonance enterography performed 12 months before surgery.

Zanon and colleagues utilised a 1.5 Tesla MRI scanner (Siemens, Munich, Germany); the acquisition protocol included T2 GASTE, ADC, T1 VIBE arterial, and late phase. Consequently, two expert radiologists, blinded to clinical outcomes, manually drew a region of interest along the involved intestinal tract in each slide. A volume of interest was obtained, and the LIFEx (Copenhagen, Denmark) software was utilised to analyse the voxels within the entire volume of interest. Based on histological results, they extracted 164 textural parameters. The patient population was split into three groups based on the Fibrosis Score where Group 0 had six patients with absence of fibrosis, Group 1 had 26 patients with mild-to-moderate fibrosis, and Group 2 had three patients with severe fibrosis.

"Researchers aimed to investigate whether texture analysis of magnetic resonance enterography could detect intestinal fibrosis in patients with CD."

The textural parameters were compared among the three groups. Ultimately, the researchers identified eight parameters that were statistically significant in defining the presence or absence of fibrosis. They concluded that MRI texture analysis could correlate with histopathological data in patients with CD with fibrotic stenosis. Zanon suggested that future studies should investigate whether the parameters could define the grade of fibrosis, rather than just the presence or absence.

Magnetic Resonance-Planimetry in Multiple Sclerosis: A Viable Alternative Biomarker?



NEW research into the use of magnetic resonance-planimetry as an alternative biomarker to predict clinical disease severity and progression in multiple sclerosis (MS) was presented at ECR 2023. With neurodegeneration being a major known factor in brain volume fluctuation and permanent disability, current methods of background atrophy measurements have drawbacks, and there is no accepted methodology for the clinical use of volumetric measurements.

Stephanie Mangesius, Department of Neuroradiology, Medical University Innsbruck, Austria, explained the methodology of this study, which included a cohort of 92 patients with MS, 65.6% of whom were female. A total of 26 patients had relapse remitting MS (RRMS) and 66 had secondary progressive MS (SPMS). Disease severity was measured using the Expanded Disability Status Scale (EDSS). The investigators assessed 1.5 and 3 Tesla T1-weighted MRIs (Siemens, Munich, Germany); planimetric measurements were performed through IMPAX EE imaging database programme; and volumetric measurements through Statistical Parametric Mapping (SPM12, Institute of Neurology, London, UK) and MATLAB 9.5 (MathWorks, Natick, Massachusetts, USA). Mangesius highlighted the volumetric measurements, which included grey matter, whole white matter, whole cerebrospinal fluid, and whole volume of white matter hyperintensities.

Spearman's rank coefficients depicted a good correlation between EDSS and ventricular variables in both RRMS and SPMS groups; however, this was observed in female patients only. A correlation was observed in females with RRMS between EDSS and corpus callosum variables, yet in the SPMS group some variables correlated strongly with males, and others with females. A similar trend was observed between EDSS and infratentorial and thalamic variables, with a notable exception in the pons area in the SPMS group, which had significant correlation in both males and females. In terms of volumetric measurements in the RRMS group, the investigators only observed an EDSS correlation with white matter in female patients, and in the SPMS group the majority of volumetric measurements correlated in male patients.

"A correlation was observed in females with RRMS between EDSS and corpus callosum variables."

Mangesius concluded the session by highlighting key trends in the results of the study, including the strong presence of sex-specific differences. The investigators have shown that magnetic resonance-planimetry can be used as an effective biomarker in the assessment of MS, with a similar clinical relevance to volumetry. Mangesius went on to identify future opportunities to improve the study, which included a prospective design, the volumetric analysis of substructures, and the inclusion of automated planimetric measures to negate bias and confirm the results obtained.

Estimating Tumour Grade in Steatotic Hepatocellular Carcinoma

TUMOUR grade, estimated through proton density fat fraction, may serve as a prognostic factor for therapy response in steatotic hepatocellular carcinoma (HCC), according to data presented by Darius Kurt, University Hospital Bonn, Germany, at ECR 2023. Kurt and colleagues questioned whether a non-invasive assessment of tumour grade was feasible through measuring hepatic fat content, allowing for a prognostic tool to help guide therapeutic decisions. Therefore, they conducted a study to evaluate the association between intralesional fat content and histopathologic tumour grade in steatotic HCC.

The team analysed data from patients having undergone a liver MRI, including proton density fat fraction (PDFF) mapping, and matched these using the database of the institute of pathology to patients with histologically diagnosed HCC within 30 days of imaging. Those having undergone treatment for HCC were excluded, as well as those who had lesions with PDFF lower than 2.2%.

Fat concentration was quantified on PDFF maps using a region-of-interest (ROC) method. The median fat fraction and tumour diameter of steatotic lesions was assessed for all tumour grades, and in case of significant differences in fat fraction between tumour grades ($p<0.05$), they conducted a further evaluation through ROC analysis. They also performed analogous subgroup analyses for patients with/without liver steatosis, as well as patients with/without liver cirrhosis.

The team noted a significant difference in median fat fractions between Grade (G)1 and G2 lesions, as well as a significant difference in median fat fraction between G1 and G3 lesions. They determined the optimal cut-off to be 5.8%, meaning that lesions with a fat fraction of 5.8% or higher are more likely to be G1 lesions rather than G2 or G3. When it came to liver steatosis, they saw a significant difference in median fat fraction between G1 and G2 lesions, as well as an almost significant difference in median fat fraction between G1 and G3 lesions. The optimal cut-off value in this case was 8.8%.

Kurt concluded that they were able to verify a relationship between histopathological tumour grade and intralesional PDFF fat fraction, and that PDFF works as good discriminator between well and less differentiated steatotic HCCs according to ROC analysis. In case of steatosis, there was an even higher effect and higher diagnostic performance of PDFF; therefore, quantification of intralesional fat content in steatotic HCCs may be a way to predict tumour grade. Future research could investigate a predictive value of intralesional fat content towards therapeutic outcome. ●

"Kurt and colleagues questioned whether a non-invasive assessment of tumour grade was feasible through measuring hepatic fat content."

Radiomics Predicting Outcomes in Patients with Metastatic Gastroenteropancreatic Neuroendocrine Neoplasms

EVIDENCE has been brought forward that highlights the opportunity radiomics can offer as an imaging biomarker to support clinicians, by standardising workflow and reducing subjective evaluation. Gastroenteropancreatic neuroendocrine neoplasms (GEP-NEN) are rare and heterogenous, and one of the main challenges clinicians experience with these diseases is assessing a reliable grading before starting therapy. At ECR 2023, radiomics was presented as an emerging non-invasive biomarker, with the ability to predict patient prognosis.

The important clinical parameters to consider during treatment are primary tumour site, staging, and grading. The Ki67 antigen is considered the strongest predictor for poor clinical outcomes in GEP-NENs. The results of a study were presented, which evaluated the radiomic approach to predicting progression in patients with metastatic GEP-NENs, which screened 71 patients and presented the data of 46 of these based on inclusion and exclusion criteria. Researchers split this cohort into two groups, stratifying progressive and non-progressive disease, and selected patients to perform volumetric liver segmentation. Statistical analyses were then performed to build a combined model of clinical and radiomic parameters that predict progressive disease, with radiomics performance tested by receiver operating characteristic and Kaplan–Meyer curves for survival analysis.

"Statistical analyses were then performed to build a combined model of clinical and radiomic parameters that predict progressive disease."

Although this combined model showed promise, the researchers acknowledged their limitations in the form of a small sample size, lack of validation cohort, and the retrospective nature of their work. The presenters concluded that radiomics can be used as an imaging biomarker predicting progressive disease in patients with metastatic GEP-NENs, based on their findings that the radiomic and combined model outperformed the clinical model in their analysis. This research suggests that radiomics could be considered as a non-invasive imaging tool to stratify patients, based on tumour aggressiveness before starting therapeutic workflow; future studies and practice are expected to shift in this direction.

Seeing Beyond Data to Actionable Clinical Insights

Support Statement: This content was created in partnership with Philips, based on information shared at a Philips-hosted fireside chat at ECR 2023.

KEY challenges facing the field of radiology today include staff shortages of up to 47%, inefficient workflows, and an increase in cost pressures. Furthermore, the workforce reports high levels of stress and burnout. The Philips fireside chat, hosted by Bert van Meurs, Chief Business Leader of Image Guided Therapy and Precision Diagnosis at Philips, Eindhoven, the Netherlands, focused on the importance of developing a connected workflow. Real-life solutions, developed through research-industry partnerships, were presented, highlighting the ways in which smart diagnostic systems can streamline clinical workflow.

Recent examples of innovation at Philips include the Spectral CT 7500, which utilises spectral imaging to provide additional diagnostic value without the need for additional scan time or radiation; the Ultrasound Compact 5000, which reduces scan time by 35%; and the MR 7700, which offers multi-nuclear imaging. Philips have developed several platforms in informatics solutions, including the Radiology Operations Command Center (ROCC), which enhances the way images are distributed by connecting experienced radiographers and the Advanced Visualisation Workspace, newly presented at ECR 2023.

Niccolò Stefani, Head of Clinical Strategy in Precision Diagnosis at Philips, discussed the increased use of artificial intelligence (AI) within the field of radiology. As imaging demand has steadily increased over the last 20 years, and is expected to grow by a further 7–10% in the next 5 years, AI remains an invaluable tool in providing insight for diagnosis. AI has the capability to provide a tailored patient approach, reducing the number of scans required to make a diagnosis. Stefani highlighted how AI can automate simple tasks, such as ensuring patients are enrolled onto screening programmes following an incidental finding during diagnosis.

Mark van Buchem, Head of Radiology, Leiden University Medical Centre, the Netherlands, and Philippe Douek, Hospices Civils de Lyon, France, discussed their recent innovations developed in partnership with Philips. Van Buchem outlined the issues associated with MRI: its high run-time and resultant high cost coupled with poor patient experience. Together with Philips, van Buchem developed a tool named SmartSpeed. By under-sampling the K space during scanning in combination with prior knowledge and AI, they were able to decrease scan times eight-fold whilst increasing diagnostic accuracy. Douek worked with Philips during the COVID-19 pandemic to develop a quantitative assessment of long disease in patients with COVID-19. AI algorithms were able to quantify long lesions and fibrosis. Douek praised the work done during the pandemic, which improved accuracy of both diagnosis and prediction of intensive care unit admission and death with just a single CT scan. ●

"As imaging demand has steadily increased over the last 20 years, and is expected to grow by a further 7–10% in the next 5 years, AI remains an invaluable tool in providing insight for diagnosis."

Radiographers at the European Congress of Radiology (ECR 2023)

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The 2023 European Congress of Radiology (ECR), with its 'Cycle of Life' theme, returned to Vienna, Austria, at its traditional time in March. There were over 1,000 radiographers registered, and the Radiographers' Scientific Sub-Committee, expertly led by Nejc Mekiš and Kevin O'Regan, had prepared an excellent selection of 35 radiographer-focused sessions. ECR 2023 achieved the highest number of on-site delegates since the start of the COVID-19 pandemic, but still maintained a hybrid format to maximise inclusivity.

ECR 2023 was unique, in that President Adrian Brady and myself, the European Federation of Radiographer Societies (EFRS) President, both work in the same city: Cork, Republic of Ireland. Ireland was a key feature of the ECR 2023 Congress, and Brady invited me to give a short speech at the Opening Ceremony, a first for a radiographer. Irish radiographers were also well represented, with a dedicated session where the 'EFRS Meets Ireland'. Within this, Michele Monahan outlined the advanced practice recognition for radiographers in Ireland, and Theresa O'Donovan discussed the radiotherapy pathway of care in Ireland.

Radiographers were also heavily involved in other aspects of the programme, for example, with 'The Cube', a dedicated space focusing on interventional radiology, and organised by Christian Loewe and Maximilian de Bucourt with involvement from the EFRS. The Cube had individual days set aside to focus on peripheral, central, oncologic, and neurological interventions. Radiographers Claire Elwood, Silvia Svetlic, and Helen Bucknall successfully presented within this forum.

In addition to a traditional lecture format, radiographers also led hands-on sessions in ultrasound. This was enormously successful, and was very well attended. Radiographers were also seen contributing to the Artificial Intelligence (AI) Theatre, where Nick Woznitza gave a talk on 'The Radiographers' View of AI in Radiology'.

Research was another strong theme within the ECR 2023 Programme. There were six dedicated Research Presentation Sessions for radiographers. This in total provided a platform for 56 multinational presentations. Themes included the future of the profession, AI, patient-centred care, general radiography, novelties in CT imaging, and radiography education. As with previous years, there was a dedicated space for radiographer-led research at the EFRS Research Hub. Within this, there were eight online surveys for on and off-site radiographers, and eight hub-based image perception studies. The EFRS Research Hub at ECR first started in 2019, and has grown exponentially under the leadership of Louise Rainford and the EFRS Research Hub Committee. A further, bigger, research hub is being planned for ECR 2024.

Radiographers at ECR 2023 also engaged in wider stakeholder events as part of collaborations with the EFRS. Radiographers engaged in conversations with the European

Institute of Biomedical Imaging Research (EIBIR), a support platform in terms of research project planning, grant support, and project management. As an example, radiographers have previously been involved in EIBIR's i-Violin and Sinfonia projects. Meetings also took place between the European Society of Medical Imaging Informatics (EuSoMII), the International Society of Radiographers and Radiologic Technologists (ISRRT), and the European Society of Radiology (ESR) Board of Directors.

ECR would not be possible without collaboration between colleagues across the whole spectrum of radiology, between radiologists, medical physicists, computer scientists, industry, and radiographers, amongst others. As radiographers, we have been made to feel enormously welcome by our colleagues at ESR, and remain deeply grateful to their staff. Radiographers, identified by the EFRS, are currently working on developing an exciting and world-leading programme for ECR 2024, entitled 'Next Generation Radiology'. The EFRS, and myself as President, look forward to welcoming many more radiographers to Vienna, Austria, in 2024.

Artificial Intelligence Solutions in Radiology Clinical Practice

Authors:	Darcy Richards, Editorial Assistant
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ARTIFICIAL intelligence (AI) was a hot topic at the 33rd annual European Congress of Radiology (ECR) 2023, held in Vienna, Austria, between the 1st–5th March. A fascinating open forum session, chaired by Martin Reim, Tartu University Hospital, Estonia, and Chairperson of the European Society for Radiology (ESR) Education Committee Radiology Trainees Forum, was held on the first day. The session, entitled 'Artificial intelligence: questions you wanted to ask us but didn't', included presentations from three experts, and focused on key questions trainees might have about AI in the field of radiology. The session covered AI performance metrics, how AI can be implemented into clinical practice, and how to start-up an AI solution business.

DEFINING ARTIFICIAL INTELLIGENCE AND ITS USE IN RADIOLOGY

Vicky Goh, Department of Radiology, Guy's and St Thomas' NHS Foundation Trust, London, UK, explained that AI is the ability of technology to perform tasks commonly associated with intelligent beings. Goh briefly commented on the evolution of AI and the increasing interest and implementation of AI in healthcare, highlighting that automated acquisition to improve standardisation; post-process deep learning reconstruction to improve image quality; and interpretation with deep learning detection on scans as the main areas that AI currently impacts radiology practice and workflows.

Goh discussed the importance of understanding algorithm performance, and explored the different performance metrics radiologists should be aware of when assessing AI algorithms, including the dice similarity coefficient as a measure of segmentation performance; plus binary classification performance metrics, including binary classification thresholds to calculate true and false positive and negatives, sensitivity and specificity, positive and negative predictive values, accuracy, and F1 scores as an average of precision and recall. Performance metrics that are independent of threshold values, including receiver operating characteristic curve and area under the receiver operating characteristic curve as a measure of how well the algorithm performs classification; precision recall curve and area under the precision recall curve as a measure of how well the algorithm performs recall and precision; and the impact prevalence has on these measures, were also covered.

The full potential of AI in radiology has yet to be achieved, and the market for AI solutions in healthcare is expanding. As such, Goh stated that having an understanding of AI and its implications is important for practising radiologists. In an emerging market, guidance on assessing AI software will be necessary to aid clinicians in decision-making when procuring these for their departments.

ASSESSMENT FRAMEWORK FOR CONSIDERING PROCUREMENT OF ARTIFICIAL INTELLIGENCE SOFTWARE

Patrick Omoumi, Department of Radiology, Lausanne University Hospital (CHUV), Switzerland, delivered an insightful presentation on a framework for how to implement commercial AI solutions into clinical practice using the

evaluating commercial AI solutions in radiology (ECLAIR) guidelines. This framework considers five key sectors for evaluating and implementing commercial AI solutions: relevance; performance and validation; usability and integration; regulatory and legal aspects; and financial and support services.

> **"Having an understanding of AI and its implications is important for practising radiologists."**

In terms of relevance, Omoumi explained that AI solutions must solve a problem, and clinicians should consider how the software would be used, the desired output, and impact on all stakeholders, keeping the anticipated end-user in mind.

With respect to performance and validation, Omoumi highlighted the importance of diagnostic accuracy guidelines for algorithm validation. Examples of these guidelines include the Standards for Reporting of Diagnostic Accuracy Study-AI (STARD-AI) and Transparent Reporting of a multivariable prediction model of Individual Prognosis Or Diagnosis-AI (TRIPOD-AI), which look at how algorithms are trained; the dataset used to train them and whether this is representative of the population it will be used on; how performance was evaluated; and whether potential sources of bias have been accounted for.

In addition to relevance and performance, clinicians should also consider usability and integration when evaluating AI software. Omoumi commented an even if an algorithm performs well, it needs to integrate with the institution’s workflow to be usable. Utilising a platform that orchestrates different types of algorithms, such as an app store, is a way to overcome institutional workload associated with integrating algorithms into workflows. Omoumi also discussed privacy concerns associated with cloud-based algorithm integration strategies, spotlighting that some institutions do not allow cloud-based algorithms despite the fact that these are easier to integrate and have better access to platform support.

Other crucial elements in algorithm assessment are regulatory, legal, and financial aspects, with regulatory bodies such as the U.S. Food and Drug Administration (FDA) and Conformité Européenne (CE) providing clearance for AI algorithms. Omoumi advised that this should be checked prior to purchasing AI software.

Pricing will be a critical point for many healthcare services, in which budgets and financial resources are stretched or constrained. Omoumi warned that given that AI solutions in healthcare is an emerging market, valuations are unstable, and vendors may increase license fees year on year, or remove their products from the market unexpectedly. As a result of this, clinicians will have to determine how much to pay for these algorithms. Omoumi discussed that performing a return-on-investment assessment is an effective method to assist in this decision-making. However, this will pose its own challenges, because the benefits of an algorithm may not be financial, but rather improved efficiency or work quality. Ongoing work to aid clinicians and institutions in determining how to pay for algorithm software will be needed moving forwards.

BENEFITS AND CHALLENGES IN IMPLEMENTING INTO CLINICAL PRACTICE

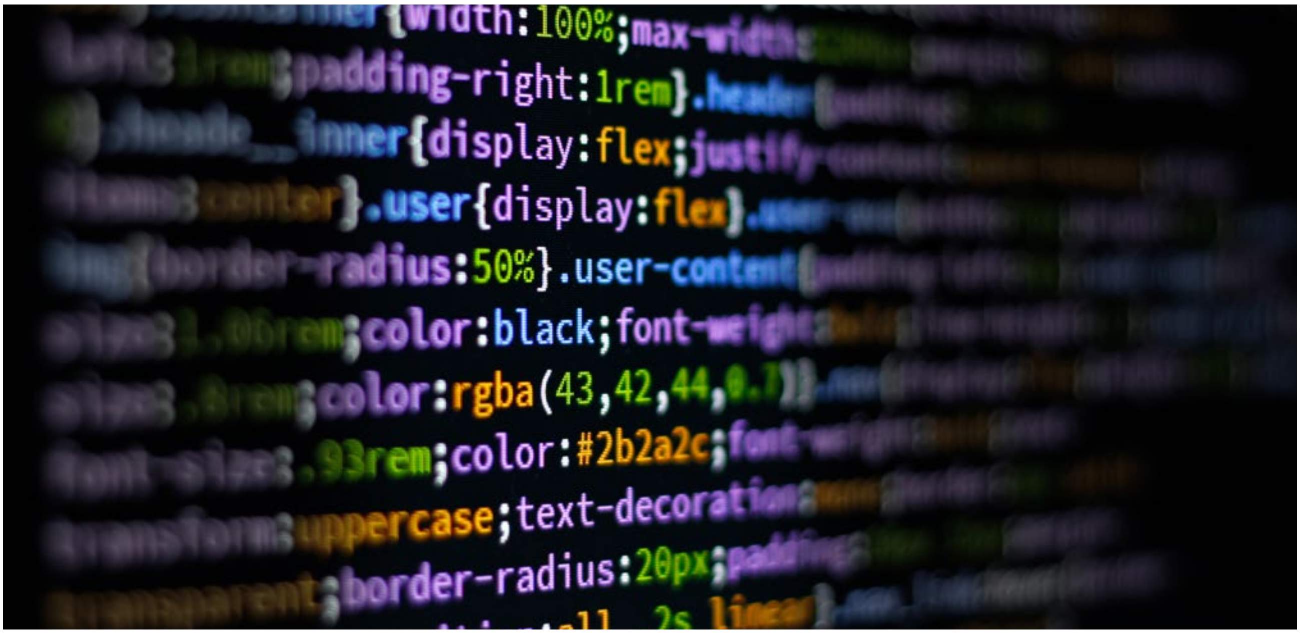
Whilst AI technology has several potential benefits for patients, healthcare professionals, and medical institutions, inevitably there are also some associated risks, both of which were explored throughout the sessions.

Goh touched on the implications of AI for practicing radiologists, spotlighting that AI may be beneficial for overcoming human error, for ensuring quality control that can be difficult in busy day-to-day practice and with a reduced work force, as well as for helping with capacity issues and workload burden. Moreover, Goh stated that AI-automated image diagnosis is projected to potentially yield annual savings of 3 billion USD by 2026.

Whilst detailing the ECLAIR framework, Omoumi discussed that the risks and benefits to all stakeholders implicated in workflows, from patients to the institution, should be considered. Benefits including increased efficiency or quality were covered, alongside risks such as missed diagnoses or misdiagnosis, given that AI solutions are currently narrow and task-specific.

Goh highlighted that one of the major benefits of AI in radiology is its ability for complex pattern recognition in large sets of data that human operators may miss, with the ability to subsequently convert these patterns into a quantitative format. Furthermore, all three experts considered how AI algorithms, such as machine learning, have the ability to improve their performance over time as they become exposed to increasing volumes of data, with Goh commenting that for specific tasks, machines are "almost achieving human-like performance" and may exceed human performance in the future.

However, there are challenges in assessing an algorithm's performance within an institution's dataset. Omoumi and Goh both discussed how AI software performance is often assessed in enriched populations, and that testing within



an individual institution's dataset often shows significantly reduced performance compared to literature-reported values. Omoumi spotlighted that performance could be markedly reduced in 25% of cases.

In addition to this, there are concerns regarding the generalisability of AI solutions across different datasets. Omoumi discussed that theoretically, an appropriately developed AI solution should perform reasonably well across different datasets, and further added that some algorithms are capable of continuous learning, and therefore able to improve their performance over time. They highlighted the importance of understanding the software limitations within an institution's dataset, and that currently, there is no way to know this information unless you perform the study yourself.

Another risk in using AI solutions is the potential negative impact on trainee education, and a reduction in basic imaging science knowledge through software over-reliance. Alongside this, there is the potential for negative impact on workflows; for example, a tool with high sensitivity and low specificity would yield a high false positive rate, increasing workload.

Validation in image segmentation was also discussed as a challenge. Goh said that noise in standalone reference data used to train algorithms due to inter-reader variability is a key concern with segmentation training. The use of algorithms capable of continual background learning alongside experts changing their image annotations in real-time as a method to perfect the segmentation algorithm could be a potential solution. However, in practice, this may be unrealistic and impractical.

CONCLUSION

AI in radiology is an exciting and emerging field, with significant potential to improve practitioner workflows and patient experiences; however, there are several concerns and challenges that will need to be addressed over the coming years. Reim closed the open forum by inviting a continued offline conversation about the topics raised throughout the session.

"In addition to relevance and performance, clinicians should also consider usability and integration when evaluating AI software."

Breast Imaging Through Different Phases of Life

Authors:	Robin Stannard, Editorial Co-ordinator
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A SPECIAL Focus Session at the European Congress of Radiology (ECR) 2023 saw global experts in breast cancer imaging come together to explore the challenges, opportunities, guidelines, and dangers of breast cancer screening across multiple stages of life. Miri Sklair-Levy, Meirav Center for Women's Health and High-Risk Clinic, Sheba Medical Center, Ramat Gan, Israel; Nuala Healy, Cambridge University Hospitals, UK; and Anne Tardivon, Department of Radiology, Institut Curie, Paris, France, shared their expansive experience, unique case reports, and novel literature to provide the audience with an examination of the nuance surrounding the screening and treating of breast cancer at different ages.

IMAGING IN FEMALES UNDER 30

Sklair-Levy opened their presentation with an in-depth examination of the complexities of breast cancer imaging in young females, defined as those under the age of 30. Breast cancer is the leading cause of death in young females, and recent epidemiological trends have shown increasing incidence in young females alongside increasing metastatic disease. While females under 40 represent 7% of breast cancer diagnosis, the annual incidence in females aged 25–29 is 8.1/100,000. Furthermore, age is the main independent risk factor for breast cancer, with breast cancer at a young age independent of poor prognosis as these females tend to have a higher risk of local recurrence. The incidence of sporadic early-onset breast cancer of unknown risk is 90% compared with only 10% coming from high-risk genetic causes including *BRCA* carriers, p53 mutations, family history, or radiation exposure. This can increase challenges as this large percentage of young females with unknown risk may not be subject to regular screening programmes.

Sklair-Levy highlighted several challenges that can impede imaging and diagnosis in young females. Pregnancy-associated breast cancer (PABC) is breast cancer diagnosed during pregnancy, 1-year post-partum, or during lactation. While PABC is rare, it has an aggressive disease course and is often associated with delays in diagnosis due to the physiological changes to the breast during pregnancy and aggressive phenotypes of oestrogen receptor/progesterone receptor negative, *HER2* positive, and triple negative cancer.

> **"While females under 40 represent 7% of breast cancer diagnosis, the annual incidence in females aged 25–29 is 8.1/100,000."**

Diagnosis is difficult as PABC often presents as a palpable lesion, which can be difficult to differentiate from common benign pathologies during pregnancy and lactation, such as fibroadenoma, lactating adenoma, galactocele, hamartoma, and abscess. Furthermore, imaging is challenging as MRI is contraindicated during pregnancy due to potential gadolinium teratogenicity; however, this can be performed during lactation. Ultrasound is the first-line diagnostic imaging modality in suspected PABC due to the lack of ionising radiation and the high sensitivity of up to 100% detection, but some cancers may appear to have benign features in ultrasound imaging, including parallel orientation, circumscribed margins, and posterior acoustic enhancement. Mammography tends not to be used

in PABC unless cancer has been proven through biopsy due to the increased breast density in pregnancy; however, it can be useful for detecting suspicious microcalcifications and for the work-up of pathologic nipple discharge.

Recent studies have examined the use of non-contrast MRI in pregnancy and summarised that this method is feasible and can detect breast cancer in pregnancy; however, the technique requires lower software resolution and is not currently used in everyday practice. Sklair-Levy emphasised the importance of not delaying imaging due to pregnancy and lactation, underlining that practice should always start with ultrasound and follow-up as necessary. Furthermore, screening in high-risk females should not stop during pregnancy, and should instead be replaced by the available modalities.

IMAGING IN THE POST-OPERATIVE BREAST

The second talk, presented by Healy, focused on common indications for imaging, features associated with cancer recurrence, and the role of imaging in the reconstructed breast, which are all key considerations for post-operative breast imaging. Healy emphasised that when considering residual disease and local recurrence, it is important for radiologists to question how they can help surgeons in addressing these risks. When looking for residual disease immediately after surgery, MRI can be difficult to interpret due to the anatomical changes, surgical enhancement, and surgical resection cavity associated with surgery. Previous studies have shown that the sensitivity and specificity of post-operative MRI can be limited (61–79% and 47–73%, respectively). However, Healy noted that an enhancing mass, a thick nodular, or an irregular enhancement of >5 mm should be considered suspicious of residual disease. Literature suggests that optimum time for a post-operative MRI is 28 days, as waiting longer does not improve sensitivity, positive predictive value, negative predictive value, or specificity. It is also essential that post-operative MRI is carried out prior to commencing radiotherapy. Healy further highlighted that these challenges underline the value of the pre-operative MRI, the indications for this being dense breasts, discrepancy between clinical examinations, and local oncoplastic techniques.

Radiotherapy has a dramatic impact in reducing post-operative breast cancer recurrence from 35.0% to 19.3%. Despite this, the risk of local recurrence. This risk is highest in the first 5 years post-surgery, peaking at the 2-year mark. This data emphasises the importance of imaging surveillance post-breast surgery, with Healy recommending annual surveillance for 5 years or up until screening age if under 50.

Signs of recurrence can include a new mass, asymmetry in architectural distortion within 2–3 cm of the resection cavity, increasing density at the scar site, increasing microcalcifications, progression of skin thickening, breast oedema, enlarged auxiliary lymph nodes, and a loss is post-surgery stability (i.e., changes between consecutive mammograms).

"Radiotherapy has a dramatic impact in reducing post-operative breast cancer recurrence from 35.0% to 19.3%."

Alongside mammography, MRI surveillance is advised for females under 50 and those with dense breasts. A recent meta-analysis study examining the benefit of MRI surveillance in all females with a personal history of breast cancer found insufficient evidence to recommend for or against surveillance MRI. Additional evidence has shown that the detection rate of mammography paired with breast ultrasound was increased over mammography alone (6.8 versus 4.4 per 1,000 women). Furthermore, the novel technique abbreviated MRI, which is MRI with a shortened diagnostic protocol, is currently under investigation with initial evidence demonstrating improved sensitivity and specificity. However, no meta-analysis has yet been carried out comparing the diagnostic performance to full protocol MRI.

Healy closed their presentation by highlighting some of the exciting prospects in post-operative imaging. Healy underscored the need for deep learning and modelling for combining several features when predicting recurrence, as well as building a risk stratification calculator for recurrence. Finally, Healy conveyed the promising prospect of abbreviated MRI and the potential this has to enable a high throughput of examinations.

IMAGING IN ELDERLY FEMALES

The final presentation, which was given by Tardivon, explored the nuanced, challenging situation of screening, diagnosing, and treating breast cancer in elderly patients. An elderly female is defined as 65–85 years; however, most clinical trials end at the age of 69 or 70, excluding a large proportion of this demographic. This means that, from a public health perspective, there are no data on screening mammography for females over 70 and on whether screening would also be of benefit for this population. Currently with a steadily increasing life expectancy and an ageing general population, more than 30% of cancers are detected in populations over 60, and 25% of cancers occur in females aged 70–74. Recent programmes in France and Scotland have extended screening age. The Scottish Breast Cancer Screening Programme now allows females to opt into continued screening to 73. Overall survival was statistically higher in the detected screened group, as well as non-breast cancer related survival.

Tardivon introduced several unique considerations that must be scrutinised when treating this elderly population. Firstly, the importance of doing no harm; longer life expectancy is a salient consideration for patients. However, radiologists must also understand that healthy life years do not always increase at the same level. When

treating this age demographic, it is essential for physicians to meet the patient and understand their status, understand their level of frailty, and decide the imaging to perform based on these factors. Patients must never be denied an examination due to advanced age alone. Several tools are available to assist diagnosis and treatment decision making in elderly patients, such as the Age Gap Decision Tool, which considers comorbidities, frailty, cancer type, and tumour size, in order to advise on the best treatment pathway for elderly patients.

Overdiagnosis is also a key challenge in elderly patients. As females age, clusters of calcifications occur. Furthermore, there are multiple misinterpretations that occur in patients over 70, and therefore radiologists need to be aware of round shaped cancers of mucinous subtype and micropapillary subtype as well as stable invasive cancers characterised by tubular architectural distortion and focal asymmetry.

Tardivon closed their presentation by emphasising the importance of treating elderly people with breast cancer with respect. Tardivon challenged the audience to take an interest in patients' lives and truly understand their level of frailty, as well as including them as much as possibly in the decision-making process and ensuring the patient understands why clinical decisions have been made.

CONCLUSION

At each stage of life, the screening, diagnosis, and treatment of breast cancer present different challenges. In young females, screening programmes are only available for high-risk populations, even though these account for only 10% of diagnoses and pregnancy can complicate diagnosis. Post-surgery MRI techniques are limited, and recurrence is high risk. In elderly females, breast cancer screening and clinical trials are often unavailable, with overdiagnosis presenting a significant challenge. These differences highlight that the age demographic must always be at the front of a radiologist's mind, and the benefits and contraindications of each imaging modality must be considered for each patient's unique situation.

Abstract Reviews

Introducing the latest research in the field of radiology presented at the European Congress of Radiology (ECR) 2023.

Interventional Treatment in Small-Sized Hepatocellular Carcinoma Using Microwave Ablation: Evaluation of Local Response and Survival

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BACKGROUND AND AIMS

To retrospectively evaluate the safety and efficacy of CT-guided percutaneous microwave ablation (MWA) of small-sized (≤2 cm) hepatocellular carcinoma (HCC) regarding therapy response and survival rates. The goal is to compare data from minimal invasive treatments like MWA and radiofrequency ablation in comparison to surgical resection or data from liver transplantation.[1-3]

MATERIALS AND METHODS

CT-guided MWA was performed in 87 patients (16 females; 71 males; mean age: 63.8±10.8 years) with 130 small-sized HCC lesions. The MWA device used was the Emprint™ (Medtronic, Minneapolis, Minnesota, USA) with the Thermosphere™ Technology Covidien (Medtronic) system. After local anaesthesia, a small skin incision was made to percutaneously insert the microwave antenna into the target lesion. Following the insertion and positioning of the antenna in the lesion under CT guidance (Somatom Sensation 64 [Siemens, Munich, Germany]), the thermal ablation was performed according to the manufactural protocol. For monitoring the ablation process, CT fluoroscopic scans were repeatedly performed.

All cases were evaluated according to axial diameter of tumour, volume of post-ablation zone, technical success, complete ablation, therapy response, overall survival, and progression-free survival. Contrast-enhanced MRI was performed post-ablation to evaluate the response to MWA.

RESULTS

The mean axial diameter of the tumour was 1.4 cm (range: 0.5–2.0 cm), and the mean post-ablation volume was 32.6 cm^3. A technical success rate of 100% was achieved in all ablations (130 out of 130). The complete ablation rate was 97.7% (127 out of 130) of all tumours. The rate of local tumour progression (LTP) was 4.6% (4 out of 87) and the rate of intrahepatic distant recurrence was 36.8% (32 out of 87). The 1-, 3-, and 5-year overall survival rates were 94.3%, 66.4%, and 53.8%, respectively. The 1-, 3-, and 5-year progression-free survival rates were 70.5%, 46.4%, and 33%, respectively. No peri-procedural deaths were reported.

CONCLUSION

Image-guided interventional treatment such as percutaneous thermal ablation is of increasing importance in the therapy of HCC. Interdisciplinary teams consisting of surgeons, interventional radiologists, oncologists, hepatologists, and radiation oncologists must decide on the best treatment option in treating HCC: surgery, image-guided thermal ablation, intra-arterial methods, or radiation therapy. For this, they need to consider location and size of the tumour, liver function, existence of extrahepatic manifestation, overall health of the patients, and patient preference.

The main challenge in treating patients with HCC by local ablative techniques such as MWA is the development of LTP or intrahepatic distant recurrence. Here, the authors showed that the rate of LTP was 4.6% (4 out of 87), and the rate of intrahepatic distant recurrence 36.8% (32 out of 87). Other authors reported rates of LTP from 8.8% to 29.2%,[4-6] while evaluating MWA of HCC.

The authors achieved an initial complete ablation in 97.7% (127 out of 130) of all tumours using MWA. Prior studies that examined MWA reported initial complete ablation rates from 71.1–98.5%.[7,8]

The authors' study had some limitations. First, it was a retrospective study and some important parameters for a well-matched study were not available. Thus, a prospective randomised study could investigate and evaluate the efficacy and safety of MWA in the treatment of HCC more accurately. Secondly, this study did not consider the possible effect of pre-treatments such as trans-arterial chemoembolisation. In addition, a multicentre study may include a larger population of patients and combine expertise from different institutes, which would evaluate this approach more comprehensibly.

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Retrospective Single Centre Study to Evaluate the Use of Targeted Radiofrequency Ablation Followed by Vertebroplasty in Difficult-to-Reach Metastatic Spinal Lesions

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BACKGROUND AND AIMS

The high incidence of bone metastases, particularly vertebral metastases, in patients with cancer and the limitations of conventional treatments are the main challenge for the interventional oncology specialty.[1,2] Several percutaneous ablation techniques, including radiofrequency ablation (RFA) with vertebral augmentation (VA), have shown promising oncological outcomes.[3-10] However, the use of straight needles in RFA has been a disadvantage for difficult-to-reach metastases.

The purpose of this study was to assess the effectiveness of a navigational steerable radiofrequency ablation device with concurrent VA in the treatment of posterior vertebral body metastatic lesions, which are technically difficult to access. Primary outcomes of the study were evaluation of pain palliation and radiologic assessment of local tumour control.

MATERIALS AND METHODS

The study included 35 patients who underwent minimally invasive CT fluoroscopy-guided percutaneous targeted RFA (tRFA) and VA for vertebral lesions from T1 to L5, with evidence of osteolytic or mixed metastatic lesions in the posterior vertebral body. Patients were classified into two groups according to the number of metastases located in the spine. A total of 21 patients (60%) had one or two metastatic lesions (Group A) and 14 patients (40%) had multiple (>2) vertebral lesions (Group B).

The minimally invasive procedure involved local anaesthesia, tRFA, and vertebral augmentation using ultra-high viscosity bone cement. Postoperative follow-up was performed with imaging at 1, 6, and 12 months to assess local activity and tumour progression. Pain severity was documented using a Visual Analogue Scale (VAS) the day before the treatment and at 1 week, 6 months, and 12 months after treatment.

RESULTS

Breast cancer was the most common primary tumour type. No neurological deficits were observed, and all procedures were well-tolerated without complications. Asymptomatic cement leakage occurred in 7.3% of treated vertebrae. No local relapse or tumour progression was observed during a median follow-up of 12.0 months for Group A and 10.5 months for Group B. The mean VAS score dropped from 5.7 (95% confidence interval: 4.9–6.5) before tRFA to 0.9 (95% confidence interval: 0.4–1.3) after tRFA, with no difference in the VAS score over time from 1 week up to 1 year after tRFA and VA. VAS decrease over time between 1 week and 1 year following RFA was similar, suggesting that pain relief was immediate and durable. Neither patients with 1–2 vertebral metastases nor those with multiple lesions showed radiological signs of local progression or recurrence of the tumour in the index vertebrae during a median follow-up of 19 months (4–46 months) and 10 months (4–37 months), respectively.

CONCLUSION

tRFA is a minimally invasive treatment that uses a steerable RFA device to target, heat, and destroy spinal metastases. The study found that tRFA with a navigation device, in combination with high viscosity vertebroplasty, can effectively control pain and tumour growth in patients with metastases also located in the difficult-to-reach posterior and the one-third of the vertebral body. The steerable navigation device allows for the precise placement of the RFA needle, which is particularly useful for reaching lesions close to the spinal cord or posterior vertebral wall. The study had some limitations, including a small sample size and retrospective design. However, the findings support the use of tRFA with a steerable navigation RFA device for the treatment of spinal metastases, particularly those located in difficult-to-reach areas. The study also highlights the importance of pain control in patients with spinal metastases, which can significantly impact their quality of life.

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Indirect Flow Diversion for Off-Centred Bifurcation Aneurysms and Distant Small-Vessel Aneurysms: A Retrospective Proof of Concept Study From Five Neurovascular Centres

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BACKGROUND AND AIMS

Treatment of cerebral aneurysms using haemodynamic implants such as endosaccular flow disruptors and endoluminal flow diverters has gained significant momentum during recent years. The intended target zone of these devices is the immediate interface between the aneurysm and the parent vessel. The therapeutic success is based on the reduction of aneurysmal perfusion and the subsequent formation of a neointima along the surface of the implant. However, a subset of aneurysms (off-centred bifurcation aneurysms involving the origin of efferent branches and aneurysms arising from peripheral segments of small cerebral vessels) often cannot be treated via coiling or implanting a haemodynamic device at the neck level for technical reasons. In these cases, indirect flow diversion (FD), a flow diverter deployed in the main artery proximal to the parent vessel of the aneurysm, can be a viable treatment strategy, but clinical evidence is lacking in this regard.

MATERIALS AND METHODS

Five neurovascular centres contributed to this retrospective analysis of patients who were treated with indirect FD. Clinical data, aneurysm characteristics, anti-platelet medication, and follow-up results, including procedural and post-procedural complications, were recorded.

RESULTS

Seventeen patients (mean age: 60.5 years; range: 35–77 years) with 17 target aneurysms (vertebrobasilar: n=9) were treated with indirect FD. The average distance between the flow-diverting stent and the aneurysm was 1.65 mm (range: 0.4–2.4 mm). In 15 out of 17 patients (88.2%), perfusion of the aneurysm was reduced immediately after implantation. Follow-ups were available for 12 cases. Delayed opacification (OKM A3: 11.8%), reduction in size (OKM B1–3: 29.4%), and occlusion (D1: 47.1%) were observable at the latest investigation. Clinically relevant procedural complications, and adverse events in the early phase and in the late subacute phase, were not observed in any case.

The indications for flow-diverting techniques are rapidly expanding; however, evidence for the endovascular treatment of bifurcation aneurysms or very small branches impeding direct probation is yet scarce, and still under debate. There is great controversy, as indirect FD demands jailing of major vessel branches, consequently affecting the haemodynamic situation; it may also alter the perfusion of the downstream territory. Therefore, it is essential to evaluate the individual collateral supply prior to the treatment, in order to decrease the risk of ischaemic events that may occur as a result of competitive flow. The study results, however, predict the indirect affection of the aneurysm perfusion as sufficient bail-out option without an increased risk of ischaemic events, and still afford adequate occlusion rates. The effect might be attributed to progressive deconstruction of the aneurysm and its parent vessel.[1] Furthermore, no increased incidence of vessel degradation as a result of FD coverage was observed.

CONCLUSION

The authors' preliminary data suggest that indirect FD is a safe, feasible, and effective approach for off-centred bifurcation aneurysms and distant small-vessel aneurysms. However, validation with larger studies, including long-term outcomes and optimised imaging, is warranted. ●

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A 50% Reduction of Radiation Dose in Dynamic Myocardial CT Perfusion with Skipped Beat Acquisition: A Retrospective Study

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Keywords: CT perfusion, dynamic myocardial CT perfusion, myocardial blood flow, skipping beat acquisition.

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BACKGROUND AND AIMS

Dynamic myocardial CT perfusion (CTP) is a relatively novel technique that can depict myocardial ischaemia. However, the radiation dose required for dynamic CTP remains relatively high. Therefore, the authors investigated the feasibility of dose reduction in dynamic myocardial CTP by comparing the diagnostic performance resulting from acquiring images during all heartbeats to that involving the periodic skipping of imaging during a certain proportion of heartbeats.

MATERIALS AND METHODS

The imaging data of 38 patients who presented at the authors' hospital with chest pain and underwent dynamic CTP on clinical indication were retrieved. All images were acquired with a 320-slice wide-area detector clinical CT system (Aquilion ONE PRISM, Canon Medical Systems Corporation, Ōtawara, Japan), and reconstructed using a deep learning-based algorithm (AiCE Cardiac, Canon Medical Systems Corporation). From the retrieved datasets, three new datasets were created in which every fourth, third, or second beat (i.e., Skip 1:4, Skip 1:3, and Skip 1:2, respectively) were removed as a surrogate of dose-reduced variants of the full-dose protocol. All datasets were post-processed using a dedicated analysis workstation.

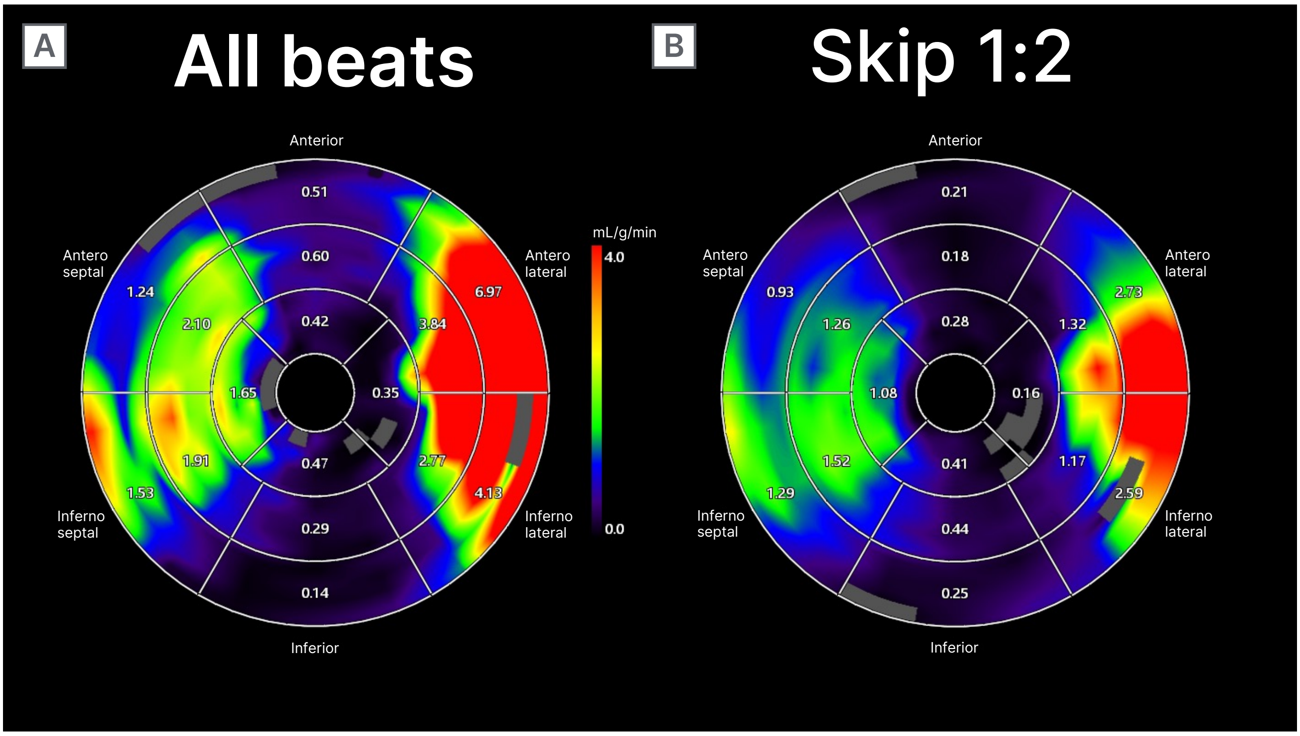
Seven radiologists with varying expertise evaluated the reconstructed CT images and perfusion maps in terms of the presence or absence of perfusion deficits per case, providing both a binary decision and a probability of deficit present rating. The latter was used to construct a receiver operating characteristics curve. The mean blood flow (MBF) in each of the 16 myocardial segments was quantified and compared per skipped-beat level, normalised by the respective MBF value for the full-dose (i.e., no skipped-beat acquisition) averaged across patients, and analysed with the analysis of variance. The number of segments and cases whose MBF was below unity (<1.0 mL/g/min) for any acquisition protocol was counted.

Additionally, the authors noted the number of maps with perfusion deficits corresponding to the stenosis on invasive coronary angiography, according to the American Heart Association (AHA) segment model. They also noted the number of non-diagnostic MBF maps (>4 mL/g/min).

RESULTS

No difference was detected in the area under the curve (AUC) based on the radiologists'

Figure 1: Comparison of the perfusion maps from all beats acquisition (A) and acquisition with skipped every second beat (B).



probability of deficit present score across datasets (p=0.44; all beats AUC: 0.73; Skip 1:4 AUC: 0.72; Skip 1:3 AUC: 0.76; Skip 1:2 AUC: 0.75) with good observer agreement (intraclass correlation coefficient: 0.8) among the readers. The average relative normalised MBFs (mean absolute error) across reconstructions were: 1.02 (0.11), 1.03 (0.17), and 1.06 (0.20) for Skip 1:4, Skip 1:3, and Skip 1:2, respectively (p=0.66).

Overall, 80% of perfusion maps (12 out of 15) showed hypoperfused regions corresponding to the coronary pathology (stenosis, dissection, and occlusion) and 20% of maps (three) had non-diagnostic MBFs across all reconstructions.

CONCLUSION

Skipping beat acquisitions, including skipping every second beat, during dynamic myocardial CTP appears feasible. Radiologist diagnostic performance did not decrease after reducing dose by removing 50% of time points in the dynamic sequence, suggesting the possibility of effective radiation dose reduction in dynamic myocardial CT perfusion imaging.

Contrast-Enhanced Cone-Beam Breast CT-Guided Biopsies in Breast Phantoms: Accuracy, Rate of Diagnostic Success, and Total Intervention Time

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Keywords: Breast cancer, cone-beam breast-CT, contrast-enhanced breast-CT, diagnostic modalities, image-guided interventions, vacuum-assisted biopsy.

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BACKGROUND AND AIMS

Vacuum-assisted biopsy (VAB) is performed when a breast lesion appears suspicious at imaging examinations. Although several different modalities can guide the biopsy, some lesions can only be visualised by imaging modalities that can depict tumour neo-angiogenesis.[1,2] For this type of lesion, MRI is the most sensitive modality when lesions are occult at second-look ultrasound or mammography.[3] However, capacity is often insufficient, and waiting lists tend to be long. In this perspective, contrast-enhanced dedicated breast CT (bCT) could be a promising, faster, and less expensive alternative to biopsy lesions that are only detected by contrast enhancement. bCT provides reconstructed, isotropic, 3D images of the breast, with high spatial and contrast resolution. When coupled with the administration of intravenous contrast agent, the modality allows for the visualisation of tumour angiogenesis. Some of the commercially available bCT scanners can be equipped with a biopsy bracket to perform bCT-guided vacuum-assisted biopsies. The 3D guidance procedure allows for the localisation, targeting, and performance of biopsies.

While two previous studies, from 2013 and 2017, showed promising results with bCT-guided VAB in non-enhancing lesions,[4] to the authors' knowledge, the potential of bCT-guided VAB in contrast-enhancing lesions has never been investigated.

The aim of this study was to evaluate the feasibility, accuracy, success rate, and intervention time of bCT-guided VAB for enhancing lesions in breast phantoms.

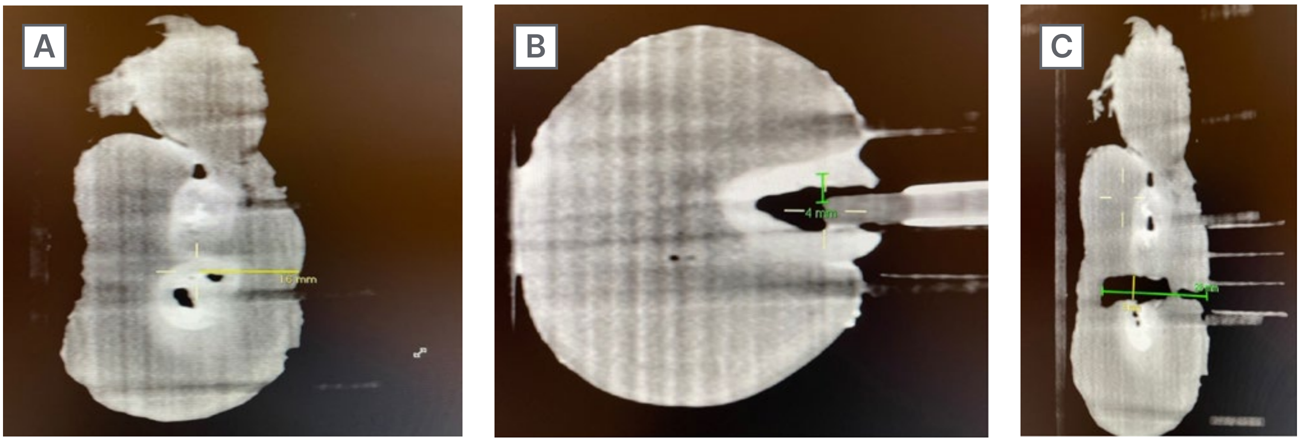
MATERIALS AND METHODS

bCT-guided VAB was performed in four different types of phantoms (chicken breast, kiwi fruit, banana, and bread) to determine the targeting accuracy in breasts of different consistency. Iodinated contrast-enhanced olives (N=10) were inserted in the phantoms to simulate enhancing mass lesions. Biopsies were performed using a dedicated bCT (CBCT 1000, Koning Corp., Norcross, USA) (Figure 1). Biopsies were performed with the 9G ATEC® Sapphire vacuum-assisted breast biopsy console (Hologic, Marlborough, Massachusetts, USA). Targeting was deemed accurate when the centre of the biopsy chamber was ≤5 mm from the predetermined target. The technical success rate (defined as olive in the sample), time for identification/targeting of lesions and tissue sampling, as well as total intervention times were documented.

Figure 1: Contrast-enhanced breast CT.

Figure 2: Olives in the sample after performing vacuum-assisted biopsy.

Figure 3: Different steps of performing a breast CT-guided vacuum-assisted biopsy.



A: Identification of the lesion on a chicken breast phantom.

B: Targeting of the lesion on a kiwi phantom.

C: Measurement of the lesion cavity at the control scan.

RESULTS

Ten 9G VABs were performed to biopsy 10 lesions. Technical success was achieved in all 10 lesions (100%) (Figure 2). During the biopsy on a kiwi phantom, needle repositioning was needed twice, as the distance to the target lesion was 7 mm and 6 mm in the first two attempts. The identification/targeting of lesions (Figure 3A) and tissue sampling took 11.5 min (10.2 min; 16.7 min) and 10.5 min (9 min; 12.5 min), respectively. The median (interquartile range) total intervention time was 22.5 min (19 min; 27.7 min). Twelve targeting attempts were needed, resulting in an accuracy of 90% (Figure 3B). For all 10 lesions biopsied, the location of the biopsy cavity was at the site of the lesion on the control scan, which was performed at the end of the procedure (Figure 3C). The median (interquartile range) size of the biopsy cavity was 14.5 mm (12.2 mm; 17.5 mm).

CONCLUSION

Success rate of bCT-guided VAB for enhancing lesions in breast phantoms was comparable to that of MRI-guided VABs reported in literature (100% versus 87–99%).[5] The median total intervention time was substantially shorter compared to that reported in literature for MRI-guided VABs (22 minutes versus 72 minutes).[6] However, these breast phantoms may not necessarily always simulate real patients, and therefore studies in patients are needed.

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An Evaluation of Zero-Click Whole-Workflow of Cardiovascular Magnetic Resonance Cardiac Function and Strain Analyses Pipeline on Cardio-Oncology Patients

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Keywords: Artificial intelligence, automated analysis, cardiac MRI, cine.

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BACKGROUND AND AIMS

Cardiac MRI provides a wealth of information for diagnosis and serial management of patients with cardiovascular disease, particularly therapeutic drug toxicity, amyloidosis, myocardial fibrosis, and oedema. The accuracy and reproducibility of cardiovascular magnetic resonance cardiac function and strain analyses from cine images are directly related to the observer's experience, and help to overcome key barriers to patient access for these management tools. Democratising patient access begins with simplifying and improving the imaging data acquisition process. The authors have engaged in the development of a fully-automated deep learning-powered analysis pipeline that starts from digital imaging and communications in medicine, and generates final reports with no or minimal human intervention. The workflow pipeline derives cardiac structure, function, strain from cine images, and myocardial texture analysis from parametric magnetic maps. Central to this overall result was the establishment of cardiac segmentation masks that could be shared with every process from cardiac function to T1/T2 maps (Figure 1). As an example, the manual segmentation of cardiac images performed by skilled human observers was compared to artificial intelligence deep-learning protocols.

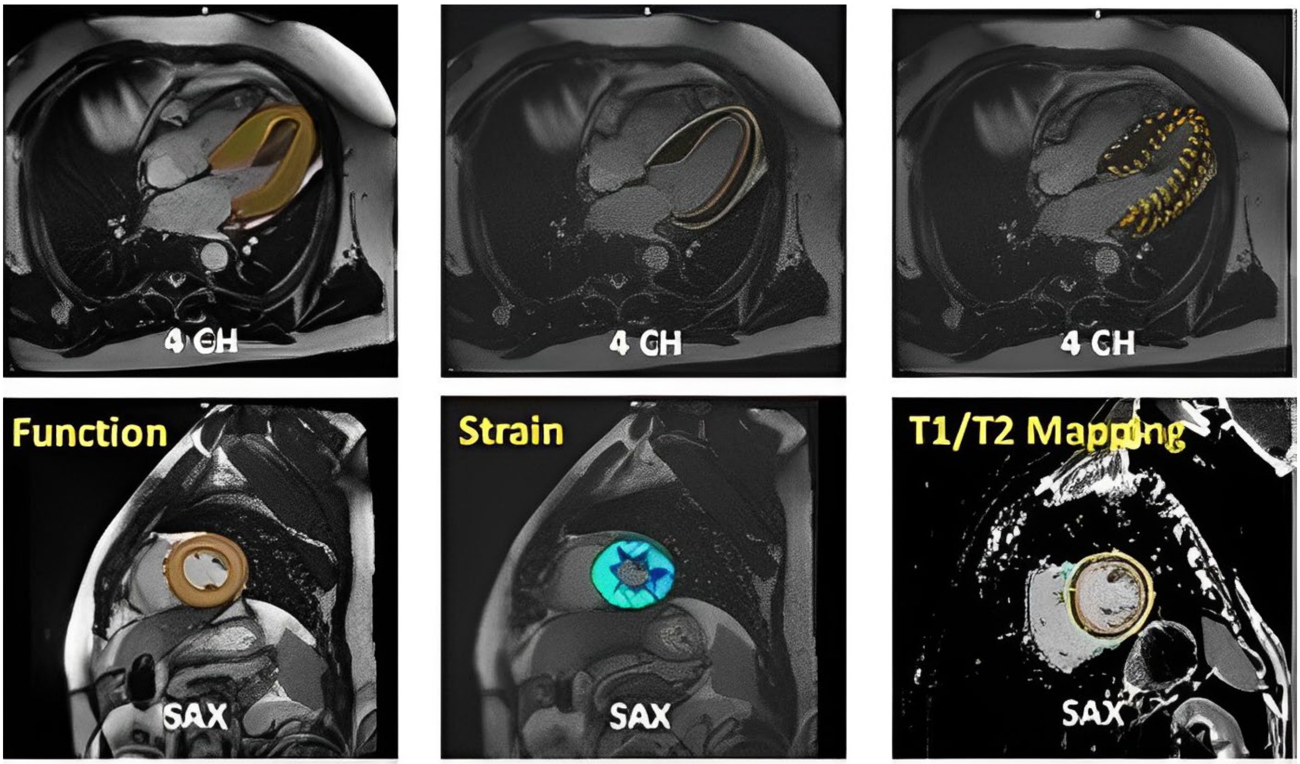
MATERIALS AND METHODS

Eleven cardio-oncology patients were scanned on a 1.5T scanner (uMR 570 scanner, United Imaging Healthcare Co. Ltd, Shanghai, China) using routine clinical protocols to acquire the multiple sequences and images. The zero-click analysis pipeline is comprised of various neural networks that detects cine images from other sequences; categorises short-axis and long-axis views; detects left ventricular (LV) range from long-axis view, and right ventricular-LV insertion points to setup the American Heart Association (AHA)'s 16 segment model; segments heart chambers and myocardium; calculates cardiac functional parameters; tracks LV myocardium; and calculates myocardium strain parameters. Two experienced medical practitioners performed the same analyses with manual editing.

RESULTS

Agreement between human observers and automated pipeline on cardiac function was excellent for LV end-diastolic volume, LV end-systolic volume, and LV ejection fraction (intra-class correlation coefficient: 0.99, 0.98, 0.98; Pearson's χ^2 test: 0.99, 0.98, 0.98, respectively).

Figure 1: Artificial intelligence feature-tracking segment cardiac borders automatically for structure, function, strain, and myocardial texture analyses.



The agreement on global circumferential strain, global radial strain, and global longitudinal strain was also excellent (intra-class correlation coefficient: 0.92, 0.85, 0.86; Pearson's χ^2 test: 0.90, 0.85, 0.87, respectively). Within-subject coefficient of variations for human observers was 4.7–16.7% for function analysis, and 14.1–32.2% for strain analysis. Within subject coefficient of variations for automated pipeline was 0.0%.

CONCLUSION

The proposed fully-automated pipeline can flow without technologist intervention to provide highly accurate and reproducible cardiac function and myocardium strain analyses compared to human observations. The proposed workflow shows the promise to be implemented into routine clinical practice to assist medical practitioners.

Development and Validation of a Radiomics-Based Decision-Making Supporting Tool to Improve the Management and Outcome of Patients with Pancreatic Cancer

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Keywords: CT, pancreatic adenocarcinoma (PDAC), radiomics.

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BACKGROUND AND AIMS

The aims of the study were to identify reliable clinical and radiomics features to build machine learning models predicting progression-free survival (PFS) and overall survival (OS), using pre-treatment CT in patients with pathology-confirmed pancreatic adenocarcinoma (PDAC).[1]

MATERIALS AND METHODS

Pre-treatment portal contrast-enhancement CT-scanner of 253 patients with PDAC were retrospectively analysed between 2010–2019. CT scans were collected from different hospitals in Belgium, with non-uniform scanner models and protocols. Demographic, clinical, and survival data were collected from medical records.

OS was used to stratify patients into a long or short survival groups (OS: ≥10 months; OS: <10 months). For PFS, patients were stratified into a long or short PFS groups (PFS: ≥3 months; PFS: <3 months). Lesions were semi-manually segmented using MIM 6.9.0 software (Cleveland, Ohio, USA), and radiomics features were extracted using RadiomiX research software (supported by Radiomics, Liège, Belgium).

Two-thirds of patients were randomly assigned to training-validation dataset, and the remaining one-third for testing.

A four-step method was applied for feature selection. Firstly, reproducible features were chosen according to recent studies on phantoms and human cohorts.[2-4] Secondly, features with good intra-rater reliability were retained based on intra-class correlation coefficient >0.75.[5] Thirdly, highly correlated and redundant features were removed using Spearman correlation coefficient >0.95. Finally, the number and names of selected features for the final models were chosen using the wrapper method (WEKA software version 3.8.6 [University of Waikato, Hamilton, New Zealand]),[6,7] which finds the best combination of features using a defined classifier (random forest classifier). This procedure was applied in the training-validation dataset with three-fold cross-validation.

Based on random forest, different machine learning models were trained and tested to predict OS and PFS. Model performances were assessed using receiver operating characteristic curves and associated area under the curve (AUC). The AUCs were compared using the DeLong test. Significance was set at $p<0.05$. This part of the pipeline was computed by using SPSS version 28.0.1.1 (IBM, Armonk, New York, USA) and WEKA software version 3.8.6.

RESULTS

A total of 171 radiomics features were extracted. Out of these, 36 features were retained after assessing inter-scanner reproducibility; 28 features were kept based on intra-rater reliability; and, after evaluation of highly correlated features, 18 features were included. Finally, using the wrapper method, six feature subgroups were selected (clinical and radiomics features, clinical features, and radiomics features [both for OS and PFS]).

Subsequently, six random forest models were trained and tested. The Clinical&Radiomics model was the most predictive for both OS (AUC: 0.75) and PFS (AUC: 0.66). Other models reached lower AUCs (Figure 1 and Table 1).

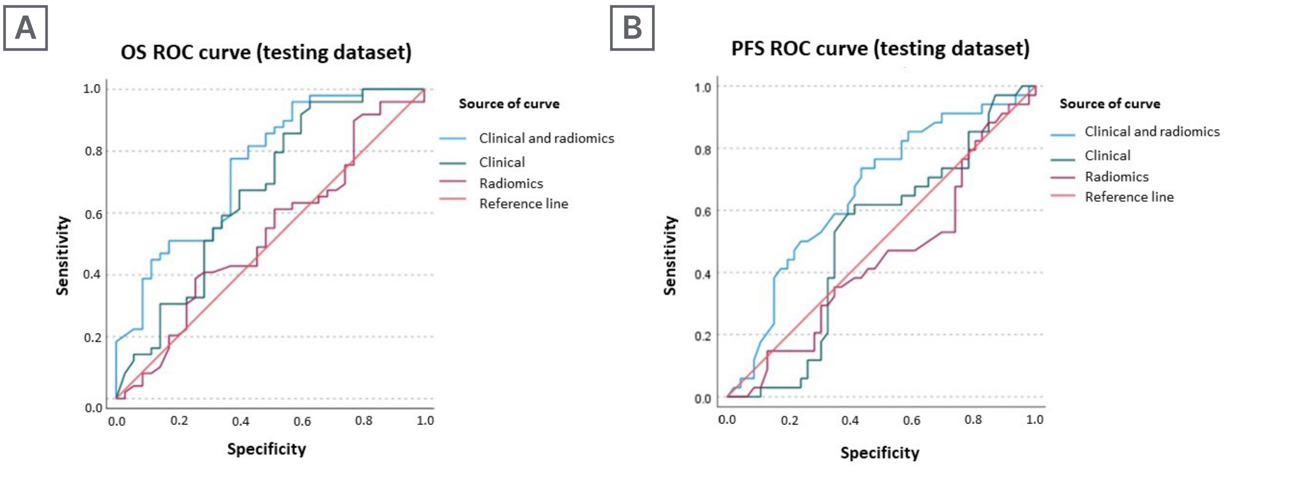
It is worth noting that the Clinical&Radiomics model for OS prediction included six clinical features and one radiomic feature (GLCM_homogeneity1);[8,9] while the Clinical&Radiomics model for PFS prediction included four clinical features and two radiomic features (GLCM_invDiffMomNor[9] and Stats_mean).[10]

CONCLUSION

Radiomics is an emergent methodology that can be used to predict outcomes. In PDAC, a combination of clinical and radiomics features reached better performances.

Given the significant variability in acquisition protocols and scanners among patients, it is crucial to investigate the reproducibility and repeatability of radiomics features, particularly in the absence of harmonisation techniques.

Figure 1: Receiver operating characteristics and area under the curves for overall survival (A) and progression-free survival (B) prediction of the different models.



AUC: area under the curve; CI: confidence interval; OS: overall survival; PFS: progression-free survival; ROC: receiver operating characteristic.

Table 1: Area under the curve for overall survival and progression-free survival prediction of the different models.

	OS (AUC [95% CI])	PFS (AUC [95% CI])
Clinical and radiomics	0.750 (0.643–0.857)	0.661 (0.539–0.783)
Clinical	0.670 (0.543–0.790)	0.510 (0.380–0.640)
Radiomics	0.529 (0.401–0.657)	0.445 (0.316–0.574)

AUC: area under the curve; CI: confidence interval; OS: overall survival; PFS: progression-free survival.

Future direction of the current project will focus on other outcomes, such as genetic, histological data, and response to treatment.

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Congress Interviews

EMJ spoke to two key players at the European Congress of Radiology (ECR) 2023, European Society of Radiology (ESR) President Adrian Brady, and European Federation of Radiographer Societies (EFRS) President Andrew England, who shared insight into the society and their opinions about key issues in both radiology and radiography.

Featuring: Adrian Brady and Andrew England

ECR 2023

Adrian Brady

European Society of Radiology (ESR) President; Mercy University Hospital, Cork, Republic of Ireland; Clinical Professor of Radiology, University College Cork, Republic of Ireland

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Q1 You attended medical school in Dublin, Ireland, before training as a staff radiologist in Canada. Do you feel that travelling was an integral part of you making it to where you are today?

Absolutely! In the Irish Healthcare System, people usually do a few general years of training after their medical school graduation in Ireland, and then do a number of years of further training in a specialty, equivalent to a North American residency. This is what I did in Dublin. After I completed my fellowship training in Ireland and passed the Fellowship exams, I moved to Canada. It is typical for people who aspire to consultant posts in Ireland to spend a number of years working abroad, and it is encouraged by training bodies. As someone who has headed up a postgraduate training body in the past, I am acutely aware of how valuable international experience is to our healthcare system. For decades, we have very successfully populated our system with people with high-level training at the cutting edge in other countries, possibly with tools or access to facilities that might not have been available at home. This has kept the standard of Irish consultants extraordinarily high.

For me, I enjoyed living and working in Canada. I found it a very congenial and welcoming place to live and work, and my wife and I retain close ties with the country. I found their healthcare system quite different in its structure to the Irish system, and that in itself was valuable, because it is always good to see how someone else does something. I think working and training abroad broadens your horizons, which is why I would encourage young radiologists and other young doctors to do it.

Q2 Your previously held the role of Chair of the European Society of Radiology (ESR) Quality, Safety, and Standards Committee (QSSC) before your current role as ESR President. Could you tell us a little bit about your previous role, and how working within that society led you to where you are today?

The QSSC is a very wide umbrella that encompasses a variety of subcommittees and activities in different areas, making it an interesting committee to chair. It was really fascinating for me as somebody who had been very familiar with the ESR, but had not previously been directly involved in the leadership. It gave me a way of understanding the breadth of the activities that the ESR undertakes, and the range of things that are going on, much of which I had not known about until I took on that role. The leadership roles in the ESR are elective, so every year vacant committee chairs go up for election among the membership. After 3 years as QSSC Chair, I ran for election as 2nd Vice President, and was successful in that.

When you are a Committee Chair and on the Executive Council, you are exposed to the wide range of activities, and get a sense of how the society works. I think the ESR has been very successful in leadership in a lot of the areas that are covered by the QSSC. For example, we have done a number of position papers on ultrasound training and ultrasound standards that are really helpful and important. The Ultrasound Subcommittee very successfully produced a white paper defining how ultrasound should be done, promoting standards. Radiation protection is a hugely important aspect of any radiologist's life. We had a Radiation Protection Subcommittee that set a number of standards, and produced a lot of white papers and position papers. That has now been merged with our EuroSafe Imaging Initiative, which is our broader radiation protection initiative, and has been running for 10 years now.

eHealth and informatics have become increasingly important as artificial intelligence has developed and become more common in radiology. This subcommittee has produced a number of very useful position papers and standards under the artificial intelligence umbrella. The Audit and Standards Subcommittee has been very active in promoting clinical audit across Europe. The fifth subcommittee, Referral Guidelines, is the one that deals with clinical decision support. It

"eHealth and informatics have become increasingly important as artificial intelligence has developed and become more common in radiology."

has been very useful to strengthen our clinical decision support software and our standards of how reports should be generated, and how clinicians should be guided to utilising the appropriate investigation for a given clinical scenario.

All of these subcommittees sit under QSSC; they have all been doing a large amount of work over the years, much of which is not always immediately realised by the membership, but which has been very instrumental in improving the standard of what we do. I found the 3 years leading that committee valuable in terms of learning what was going on, and in terms of my assisting the subcommittees in getting the message out there, and getting their work programs carried through to success.

Q3 As discussed, you have held many roles in radiological societies. Can you talk about the value you feel these societies provide, both for clinicians and patients themselves?

For 11 years, I was a member of the board of the Faculty of Radiologists of The Royal College of Surgeons in Ireland, which functions in two ways. It is the National Society for Radiology in Ireland, and it is also the body that runs and sets the standards for, and manages all specialty training in radiology and radiation oncology. In many countries, the national societies are representative societies, and training is separate from that; however, our faculty has a very central role in actually running the residency training programmes as well.

Towards the end of my time, I served 2 years as the Faculty Dean, the equivalent of president of the society. I found this very fulfilling, and it helped me get to know how things happen on a national level, and how those national practices and standards compare to what goes on elsewhere. It also gave me a lot of good experience in terms of running structures within an individual country. After finishing my term with the faculty, I became quite involved in the European Diploma in Radiology, which is run by the European Board of Radiology. I was a participant as the European Diploma Exam developed, expanded, and changed its structures to accommodate the need to deliver on multiple sites with larger numbers. I suppose that led to my interest in becoming involved directly in ESR leadership.

So, how do these things help patients and clinicians? I am going to answer this in the context of how this benefits practitioners, doctors who practice in different medical specialties. I think having a strong specialty society within a country, or supranationally, such as the ESR, is vital in terms of setting standards, sharing information, promoting research, and promoting development of specialties. I do not think there is a doctor in the world who would not recognise the benefits that accrue to their specialty, and into their practice, from having strong professional societies.

Patients often are blissfully unaware that societies like this exist, unless we actively engage with them. But again, their interests are very much served by societies like the ESR, as they maintain standards and increase education, ensuring protection of patients, and safety in everything that is done. We have a very strong Patient Advisory Group that we consult for most of our activities, to give us very valuable inputs in guiding us, to ensure that everything we do is patient-centred. While patients are often unaware we exist, I think the standard of care we provide is hugely influenced by strong active societies like the ESR.

Q4 In your 2023 ECR Foreword, you spotlight the Trainees in Focus programme. Could you explain to our readers why you feel this programme is such a valuable part of ECR 2023?

For the last 3 or 4 years, we have focused on one specific group at each congress. This helps us plan part of the programme to specifically look to the interests of those groups. For example, in the past we've had children, patients, and women as the focus group. This year, I thought it would be helpful to highlight trainees. My career is in its latter stages, and many of the people who achieve leadership positions in societies are those with a lot of their career behind them, rather than ahead of them. A lot of the attendees at the ECR are our younger colleagues. So, I wanted to focus on that, and in particular on the people who have yet to achieve independent practice, who are still training or doing their residency training, or equivalent. In addition to the usual educational material, the Trainees in Focus programme will be looking at aspects of how their working life may look in the future: things like the dangers that flow from commoditisation of radiology, the impact of artificial intelligence on how radiologists work, and considerations of work-life balance, burnout, and how the working life is changing and may change in the future. We want to teach people how to adapt to change to ensure they can be as effective as possible, and enjoy the practice of radiology as much as possible.

Having a focused programme like that will, I hope, be of great interest to our younger colleagues, and I hope they will learn useful tips and tricks and contribute to the conversations, in terms of how they want to see the specialty develop in the future. In 10 or 20 years' time, they are the people we will be relying on to lead, and to provide radiology services.

Q5 We last spoke to you in 2020, in the midst of the COVID-19 pandemic. Can you talk about how ESR has changed, and what lessons were learnt throughout the pandemic?

In terms of the congress, I think everyone is aware of the rapid changes the ESR has had to adapt to due to COVID-19. As many readers will recall, 2 weeks prior to the 2020 congress we were obliged to take the decision to cancel the on-site congress and move it to the summer, and ultimately to an online format. Many countries entered lockdown at some stage in March 2020. A very wise decision was taken by Boris Brkljačić, who was the President at the time; Peter Baierl, our Executive Director; and all the staff involved, not to hold an on-site congress in 2020, and ultimately to move it online. That required a huge pivot on the part of everybody involved: the very talented office staff that put the congress together every year, all the speakers and moderators, and all the attendees. Despite the rapidity with which these changes needed to be made, they were made very successfully, and within the limits of what is possible, we had a great online congress in July 2020.

In 2021, we were allowed to plan slightly further ahead, but again, there was uncertainty. Ultimately, we held a short event in March and a fuller online congress in the summer. Since we had more time to plan, and had acquired expertise rapidly in 2020, we were able to plan a larger online congress than in 2020. In 2022, again, it would not have been possible to bring people together safely in large numbers in March. We therefore held an online Overture Congress in March, a new venture for the society, a different style. We introduced round-table type discussions, where topical issues were discussed by experts, and broadcast to our membership. They proved extremely popular and very helpful to a lot of people. We then had a very successful on-site congress in July. It has been decades since the Society met for congress in the summer and that was a lovely experience.

The last 3 years have been hectic in terms of accommodating changing circumstances, but the Society has learned an immense amount from it. Our capacity to livestream multiple streams of activity simultaneously, and to reach our audience, whether they are physically present or online, has grown hugely. We are bringing all that forward into future congresses. ECR 2023 will be in person in Vienna. We are hoping for a very strong in-person attendance, but everything will be livestreamed as well, and people can register and attend online should they wish. They will not be able to participate in the social and networking element of the congress, but from an educational point of view, we are now capable of streaming all the educational content live. We were doing some of it before COVID-19, but now we are able to do it better, and more broadly.

Q6 As ESR President, what do you see as the future priorities for the Society and the Congress?

They are interlinked, of course, and I will not separate them. Next year's congress will be under the presidency of Carlo Catalano. The programme planning committee for ECR 2024 is already in train, and planning is underway. The priorities for the society are to remain as present in the lives of our members as we possibly can, and to offer them guidance and leadership as the world changes around them.

We have over 130,000 members now, from 186 countries, so we are a global organisation in many respects. While we are a European Society, many of our members come from way beyond Europe. We are learning a lot from member institutions, member societies, and individual members from elsewhere. Equally, there is a large amount that we can disseminate throughout our membership within and outside Europe, in terms of information and liaison with policy setting bodies like the European Commission.

We do not have to change much of what we do, because our society has been hugely successful and continues to be. I think we have to maintain the steady increase in our reach and maintain the hard work we have been doing for many years to guide the development of radiology and radiologists, through the training, standards, and education we have been offering for many years. I am a firm believer in the 'if it ain't broke, don't fix it' model. If you have something that is working very well, always look at the marginal gains that you can achieve in terms of tweaking things, but do not change things just for the sake of change.

I have explained how much we have learned over the last couple of years, and how much we had to adapt. What I want to see happen is the congress return to full on-site attendance. I do not know if we will get back to the numbers that used to attend on a regular basis every year before COVID-19. But I want to ensure that we continue to reach those numbers of people and even more, whether on-site or online. In terms of priorities, my goal is to ensure that we continue the success that we have achieved over many years.

"I think having a strong specialty society within a country, or supranationally, such as the ESR, is vital."

Andrew England

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Q1 What initially led you to pursue a career in radiography?

I think there were two reasons I chose radiography. I was always interested in technology when I grew up; anything that had a plug on it, or anything that was the latest technology, I was interested in and wanted to try out. But I also enjoyed the idea of caring for people, so radiography was a good opportunity to mix technology with patient care. I did a physics course at school, and they suggested you went to the local hospital to look at their X-ray department. That is when I found this career as a radiographer. I then applied, went to university, and since 1999 have been working in the field of radiography.

Q2 Do you think that there are any misconceptions about the speciality of radiography?

The first misconception is that radiographers just take the X-rays, but the role is much bigger than that. Radiographers perform CT and MRI scans, undertake fluoroscopy, nuclear medicine, ultrasound, and bone density examinations. We are pretty much involved in every aspect of medical care, from injuries to cancer imaging, and imaging from birth until, and beyond, death. Another misconception is the difference between radiology and radiography. The main difference is that radiology or radiologists are medically qualified doctors that have received specialist postgraduate medical training in interpreting radiology examinations, and providing a formal diagnosis. Radiographers traditionally did not do this. Radiographers were responsible for acquiring the images, and a medical doctor would then interpret and write a formal report. But now, more and more radiographers have been trained to do some of that report writing, although radiologists would lead on the more complex examinations. So, these are the two main misconceptions: the scope of the role, and the difference between a radiologist and a radiographer.

Q3 How does the European Federation of Radiographers Society (EFRS) use its position to educate practitioners about the field of radiography?

The EFRS represents over 120,000 radiographers across Europe, and in doing so, it represents over 40 national societies that represent radiographers in their home country. But it also works closely with over 60 educators, and it really has an enormous reach in terms of informing people on what is currently happening in radiography and what are best practices. It is a great forum for people to be inspired and think: "Why can't we do what they're doing in a particular country?" People look to the EFRS for that kind of vision and leadership. We have a number of opportunities where we seek to inform and develop our membership, including at the European Congress of Radiology (ECR).

Q4 What are the most exciting changes to the scientific programme for ECR 2023 compared to ECR 2022?

I think one of the main things is that we're going to be more on-site and in person than we have been since the start of the pandemic. ECR 2022 was on-site, but some countries still had travel restrictions. Hopefully now we are going to see more and more people, more and more of our colleagues and friends, that we used to see at previous ECR congresses.

> "Although some sessions at ECR are branded as radiographers' sessions, they are open to everybody."

Something I am particularly excited about is that the radiographers' content has grown, and we are very grateful to the European Society of Radiology (ESR), and Adrian Brady, for the support they have given. The radiographers' programme is largely going to be delivered in one area of the conference centre, where there will be a radiographers' lounge and a lecture theatre. There will also be a research hub, which is almost like a science room, where people can go and get involved in some of the latest experiments around radiography. If you want to find out what research is being done, not only can you go in that room and see it, but you can actually be part of it. So, we are really excited about that. This concept is not new, but it has grown considerably. In fact, a lot of the changes are more about growth; we know the things that work well, and we've expanded on them.

Q5 You are a member of the Postgraduate Education Programme Subcommittee, and a Section Coordinator of the Open Forum Programme. Could you please explain what these positions entail, and how they contribute to the success of ESR?

These positions are really about representing the entire radiography community of Europe and beyond, and suggesting ideas for topics and methods of delivery. Within the Postgraduate Education Subcommittee, it is all about putting ideas forward and trying to provide the voice for radiographers, but also listening to colleagues across different specialties about how areas or content can be improved, and giving them feedback. The meeting is truly multidisciplinary, as there are radiologists, medical physicists, and radiographers on the committee. As a committee, we listen to each other and we share ideas, whether that's for speakers, topics, overall sessions, or titles.

Although some sessions at ECR are branded as radiographers' sessions, they are open to everybody, and often we will see people dipping in and out from the different specialities. The Open Forum at ECR 2023 is designed for people to be able to drop in and out, allowing radiographers to see the latest research in a very open and positive environment. ECR is an excellent congress for those who may not want to be at a session from the beginning to the end, but prefer to drop in and see two or three talks and then move on to the next. The ECR 2023 App allows you to plan your agenda for the week, and move between meetings and sessions.

Q6 As an educator, where can we expect to see your focus lie in the coming years?

I recently gave a talk at the Arab Health Total Radiology conference about the future of radiography, and I think there are a few key areas where we are going to see greater focus: education, and how we embrace technologies, particularly those which are computer-based. We need to learn how to embrace the benefits of computers, artificial intelligence, and machine learning for our patients. We are often scared that technology will make us less efficient, or will not clearly help improve patient outcomes. But if we use these technologies correctly, then we have got a good opportunity to improve patient care, and to improve the efficiency of our practice. So, it is about focusing on embracing new technologies positively.

Q7 What are the most significant changes you have seen in the speciality of radiography during your time working in the field?

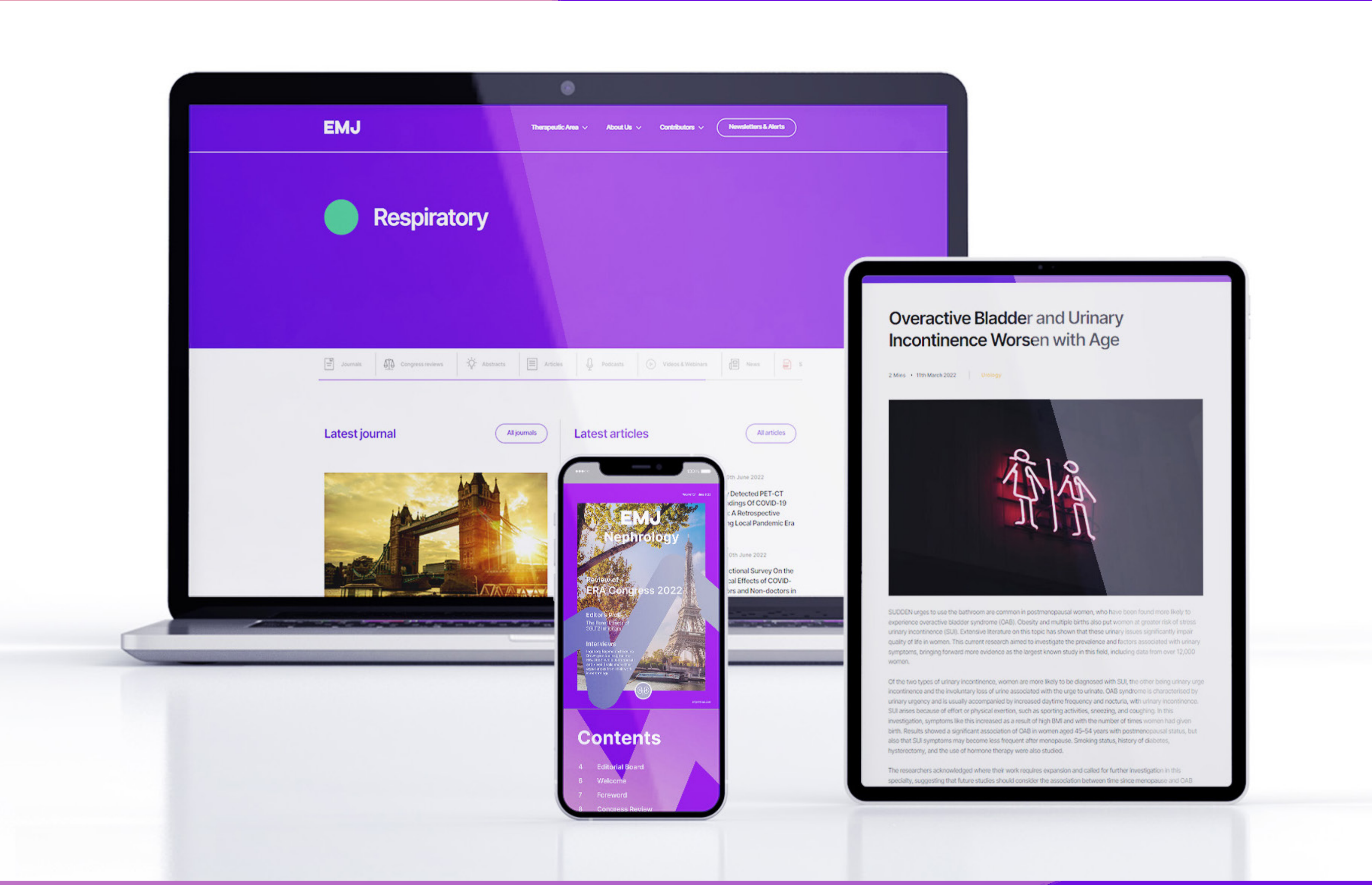
I would say there are two areas to focus on here. The first one is digitisation, or the computer revolution. When I started as a radiographer, 20 years ago, all images were hard copy X-ray films. Over the past 20 years, we have seen enormous changes in how we acquire and view radiology images. Everything is now paperless and digital. Images are reviewed on computers or tablets, and they can be reviewed throughout the hospital, or remotely. This technology has allowed for more conditions to be diagnosed, and for newer treatments to evolve. I would really say the digitisation would be the main one from the technology side.

The second one would be how our role as a radiographer has changed. While radiographers still acquire X-rays, images, scans, and so on, we are now also starting to write formal radiology reports, perform some of the advanced examinations, and maybe even perform some small treatments, such as taking a biopsy or inserting a catheter into the central venous system for feeding, or to provide medication. The role of radiographers is growing, and the range of career options is now much vaster.

Q8 Are there any innovations on the horizon of the field of radiography that you think are particularly noteworthy?

Again, there are two areas of change. Technology is continuing to grow, and it is going to allow us to take medical images with lower doses of radiation. This has always been a big restriction. While radiology is very powerful in terms of helping in medicine, you have to use it carefully. However, the radiation doses are decreasing, and we are going to get to a point where scans that are currently kept for very selective indications or very serious conditions will have doses similar to standard X-rays. So, we might actually see that we're doing much more cross-sectional imaging (CT) and maybe less conventional radiography (X-rays) in the future. Similarly, one of the limitations with MRI scanning is time; typically it can take around 30 minutes to acquire a single scan. This means that you are limited in terms of how many scans you could offer in a day, and also makes it only accessible to certain patient types. Now, there is evidence that we can offer scans that are in the region of 1 or 2 minutes. This will mean that the amount of scans that can be offered will be greater, and that different patients will be able to access them. We are probably going to see some changes in what we would normally call first-line imaging. While that area commonly focuses on X-ray imaging, you might start with more CT or MRI examinations. The other area is advanced practice. The role of radiographers and radiologists is going to continue to change over the next 10–20 years, especially with the more widespread availability of artificial intelligence.

"The EFRS represents over 120,000 radiographers across Europe."


EMJ
Respiratory
Latest journal
Latest articles
Overactive Bladder and Urinary Incontinence Worsen with Age
EMJ
Nephrology
Contents

Interview

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Q1 You initially studied biomedical engineering, and electrical engineering and medicine at Duke University, Durham, North Carolina, USA, and Yale University, New Haven, Connecticut, USA, respectively. Following this, what led you to pursue a career in radiology?

Through my engineering work, I was particularly interested in signal processing, and signals in computers are really just ones and zeros that you can manipulate mathematically. For me, the signal I chose to study was the medical image, which led me to become fascinated with radiology, and the potential that signal processing could lead to new medical knowledge through the field of radiology. When I was in graduate school, MRI and PET were relatively novel from a clinical standpoint, and I had the opportunity to see fascinating uses of MRI, PET, and CT to image patients and provide additional clinical information. For me this is where it all started, studying medical imaging signals from an electrical engineering perspective.

Q2 Do you think there are any misconceptions about the field of radiology, and what a radiologists' role in healthcare is?

I think that there are some key misunderstandings about the field. Firstly, I think a lot of people do not understand that radiologists are physicians, and that they do more than just interpret images. They are critically involved in diagnostics and patient management. As an example, in cancer medicine, radiologists have acutely nuanced relationships with oncologists, helping to determine whether lesions are improving based on imaging data or not. Through interventional radiology, the role of the radiologist is both therapeutic and diagnostic. Overall, I think of the radiologist as a signal or knowledge broker, assimilating data from the images and the medical record to provide clinicians with the best information for patient management and the patient with the best possible care.

Q3 Throughout your education and career, you have studied and worked at numerous illustrious institutions across the USA. Where do you believe that you gained the most experience, and do you believe that switching institution was integral for you to make it to where you are today?

While I stayed for many years at each institution, I do think experiencing multiple places and academic cultures can be beneficial. During my undergraduate education at Duke University, my mentor, the late Theo Pilkington, suggested that I go elsewhere for graduate school to learn different opinions and perspectives. I found my time at the University of California San Francisco (UCSF), USA, to be particularly integral to the activities I am now doing. My activities were very multidisciplinary, working with digital images and with specialists in radiology and other fields. This gave me an idea of how to go beyond the publishing of a paper, to actually implementing technologies into clinical practice. It was a wonderful experience, and a lot of fun.

Q4 You were instrumental in designing and implementing picture archiving and communication systems (PACS). Can you tell our readers more about the work required to design this system and the value it provides for healthcare professionals?

Previously, radiology practice was entirely film-based. The accumulation of imaging data was increasing rapidly, and becoming very costly to manage on film. PACS allows radiologists to acquire different images digitally, and store and transmit them digitally. Instead of individuals walking film from one place to another, we can now transmit images over networks, store images digitally, and visualise them on computers, all of which has tremendous economic and workflow benefits. This means that you could have an individual in the radiology department and someone in the emergency department looking at the same emergent imaging exam simultaneously, increasing the efficiency of patient care. Today, much of the developed world uses PACS.

> "Through interventional radiology, the role of the radiologist is both therapeutic and diagnostic."

Q5 You hold positions with several radiological societies. Can you talk about some of the work these societies do to educate radiologists and other healthcare professionals about the field of radiology?

I think it is important to participate in professional societies. I feel societies enable peers to collaborate and exchange information. I believe one of the key roles of these societies is education. The European Society of Radiology (ESR), UK Radiological Congress (UKRC), Radiological Society of North America (RSNA), and Society for Imaging Informatics in Medicine (SIIM) all share a core philosophy, which is to educate professionals. One of the most interesting things about radiology is how frequently it

changes, requiring us to adopt new technology quickly. We constantly have to teach people about these new advances. I have worked in academic healthcare institutions throughout my whole career, but many people are in private practice and they do not have the opportunity to see these novel technologies as early as we do, so I think education is extremely important to reach everyone.

Q6 What are the main aims you hope to achieve by working with these organisations?

I feel that it is the responsibility of every professional to be engaged and involved in their professional organisation. I consider it an unwritten role that one plays. I have had a wonderful time participating in these societies; for example, discussing machine learning, informatics standards, and new technologies with experts from all over the world, who have dedicated their careers to the subjects. Talking and combining knowledge with people of different backgrounds allows you to expand your knowledge and truly make an impact on a broader scale.

Q7 How does your involvement as an Associate Editor of both the *Radiology: Artificial Intelligence* and the *Journal of Medical Imaging* allow you to share your specialist knowledge about digital radiography, medical informatics, and machine learning?

I see the role of associations with journals, or at least contributing to reviewing papers, as another professional obligation. Again, this is a form of education and knowledge dissemination. As a reviewer, you see exciting papers come in that may not be articulated as well as they could be, or sometimes may have errors in methodology. You can give the authors constructive feedback, enabling them to resubmit their papers and improving the quality of the science that is disseminated. As an associate editor you are guiding authors and making sure that important information is shared, and you act as a gatekeeper to assure good science is communicated properly.

Q8 As an educator, where can we expect to see the focus of your teaching lie over the next few years?

My focus is on educating radiologists and other medical professionals on the practical, clinical aspects of machine learning. I feel our residents at Brigham and Women's Hospital, Boston, Massachusetts, USA, and Massachusetts General Hospital, Boston, USA, and all residents, should know some basic fundamentals of machine learning, know how to read the literature, implement the tools, assess the outcomes, and note problems when they arise in the applications that they use. I do not know exactly what the next technology will be, but I feel it is very important for clinicians to understand these tools that they will ultimately use clinically. We do not necessarily need them to be computer programmers, but they need some skills and a foundational background to allow multidisciplinary collaboration between data scientists, radiologists, and other healthcare providers to produce the best results.

Q9 How have you personally acquired the leadership skills to perform in your role as Director of Academic Research and Education at the MGB Data Science Office?

I have never really had any formal leadership training, but I learned on the job because I had to. I found a large

"My focus is on educating radiologists and other medical professionals on the practical, clinical aspects of machine learning."

portion of leadership was learning how to speak to people in their language, understanding what it is they needed in their positions, and how they did their work. Healthcare is so vast and complicated that you cannot possibly be an expert in everything. It is about knowing how you can use your expertise to work together and move the whole field forward faster.

Q10 What are the most significant changes that you have seen in the field of radiology during your time working as an innovator and an educator in the speciality? And are there any innovations on the horizon in the field of radiology that you are excited about, or think are particularly noteworthy?

When I started studying signal processing and I chose medical images as my signal, we did not have digital imaging per se. Now, we have technologies such as PACS and digital radiography, and the workstations to visualise digital images, so we have this wonderful treasure trove of data to analyse. This is a blessing and a curse. Now that we have digital data and high performant computers, we can use machine learning to analyse this data. I am very interested in the translational aspect of implementing machine learning models in the clinical arena, and seeing the impact on patient care. I think this needs to be the focus for radiology: putting tools into clinicians' hands, improving workflow for radiologists, and removing human error through machine learning. These are the things I am excited about, and that I would like to continue to work on in the future.

Imaging for Targeting, Monitoring, and Assessment After Histotripsy: A Non-invasive, Non-thermal Therapy for Cancer

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WHAT IS HISTOTRIPSY?

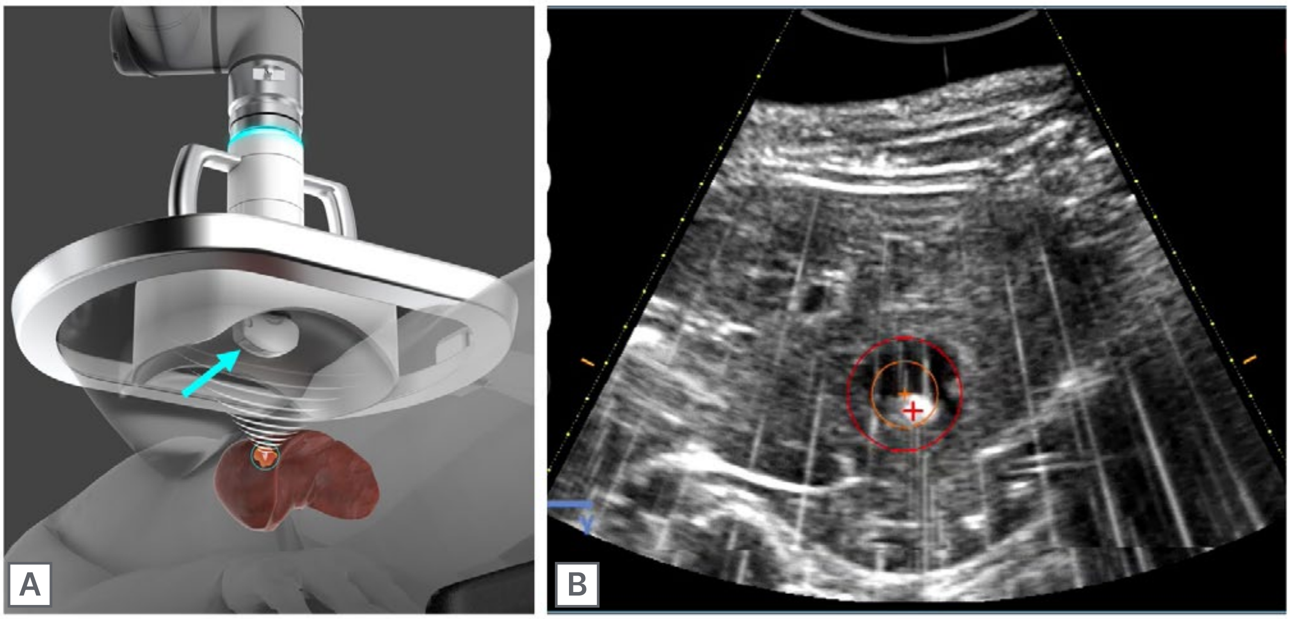
Histotripsy is a non-invasive, non-thermal, and non-ionising focused ultrasound (US) treatment method that destroys tissue through mechanical disruption caused by cavitation. Short-duration (<20 μs) high-pressure US pulses cause the rapid expansion and collapse of endogenous gas bubbles in targeted tissue.[1,2] This results in high local mechanical stress and strain, eventually leading to rupture of cell membranes and liquification of tissue.[3] Tissue destruction by histotripsy is a threshold effect in that a tissue-specific cavitation threshold needs to be reached before cavitation and tissue damage occur.[4-6] Certain collagen-containing tissues with high mechanical strength, such as ureters, bile ducts, and large blood vessels, are relatively resistant to damage from histotripsy compared to highly cellular parenchymal organs and many tumours.[7] Treatment zones are characterised by precise margins, no damage to intervening tissues, and acellular debris within the treatment zone that is rapidly resorbed.[8]

Histotripsy differs from high-intensity focused US thermal therapy due to the non-thermal (mechanical) nature of histotripsy and the threshold effect that increases precision, spares certain structures with high mechanical strength, and avoids tissue damage outside of treatment zones.[4] Another potential benefit of histotripsy versus thermal methods is the post-treatment preservation of neo-antigens, which have the potential for immune stimulation.[9-11] Histotripsy does not appear to increase the risk of parenchymal haemorrhage, even in anticoagulated subjects.[12] To date, histotripsy has been applied in small clinical trials for the treatment of benign prostatic hyperplasia and malignant liver tumours,[13,14] and larger trials are currently planned or underway. Multiple future applications are being actively explored in preclinical models and include treatment of benign and malignant tissue in the liver, kidney, pancreas, brain, thyroid, subcutaneous fat, and blood vessels.[10,15-21]

This manuscript focuses on the imaging surrounding histotripsy, a technique that uses microsecond pulses to generate inertial cavitation. Boiling histotripsy is a related technique that uses millisecond US pulses to generate boiling bubbles to liquefy target tissue.[22,23] Boiling histotripsy is not yet in clinical use in humans, and the similarities and differences between the techniques are beyond the scope of this review.

Successful histotripsy treatment depends on accurate and precise image guidance. Diagnostic US is currently used to target and monitor histotripsy. The current histotripsy device being prepared for human clinical use consists of a diagnostic US transducer co-axially aligned with the larger therapeutic treatment head (Figure 1). Cavitation produced by the therapy transducer forms an echogenic focus in tissue (Figure 1), which enables the diagnostic transducer to be

Figure 1: Histotripsy treatment head.



A) The therapeutic US transducer is co-axially aligned with a diagnostic US transducer (blue arrow), which can be used for planning and monitoring of the treatment in real time. **B)** The bubble cloud appears hyperechoic on B-mode US and is visible during histotripsy treatment of a healthy swine liver. During planning, the treatment zone is selected (red circle) and the bubble cloud is aligned to the crosshairs (red crosshair). Treated tissue within the red circle appears hypoechoic.

US: ultrasound.

used for targeting, monitoring, and limited post-treatment assessment.

MRI and conventional CT guidance cannot currently be used to guide histotripsy. The robotic arm, treatment head, diagnostic US transducer, and coupling water bath of current clinical systems will not fit into the bore of either conventional CT or MRI. In addition, the robotic arm and US transducer components are not currently MRI compatible. However, future development of both CT and MRI guided histotripsy systems is anticipated as components decrease in size and become MRI compatible. Fusion imaging between a pre-procedure CT or MRI and the co-axial diagnostic US transducer is possible; however, limitations such as tissue deformation from water bath compression, respiratory motion, and peristalsis may decrease the accuracy of fusion images.

ULTRASOUND GUIDANCE IN HISTOTRIPSY

US imaging provides many benefits for planning and monitoring histotripsy treatments. The co-axially aligned diagnostic transducer can be extended forward for direct contact with the body wall, which provides better image quality than a stand-off transducer in a water bath. Advantages of using US for targeting and monitoring histotripsy include real-time visualisation of the bubble cloud, multiplanar capability, and colour doppler imaging to visualise blood vessels. The fixed alignment of the therapeutic and imaging transducers is a particular advantage in that the focal zone of the therapeutic transducer remains in the field of view of the diagnostic transducer regardless of the position of the treatment head.

Cavitation bubbles created by histotripsy are echogenic on B-mode US and are an effective surrogate for cavitation forming in tissue (Figure 1). The visibility of the cavitation bubble cloud is useful for several stages of the planning and treatment process.

For treatment planning, a series of test pulses dispersed throughout the planned treatment zone are used to determine the minimum voltage required to create cavitation. During each test pulse, the system voltage is slowly increased by the user until the bubble cloud is observed on B-mode US, indicating that cavitation is occurring. This use of test pulses assures that the minimum amount of power necessary to create cavitation is used throughout the treatment and that heterogeneous tumours are adequately treated.[24] Test pulses occur during the planning stage and do not affect the treatment time, which varies depending on the total volume to be treated. The visualisation of the bubble cloud can also be used for correction of the varying speeds of sound inherent in treating through the inhomogeneous body wall and intervening tissues.[25]

Post-treatment assessment is usually performed with either contrast-enhanced CT or MRI. However, treatment effects may also be detected by US due to histotripsy-mediated destruction of cell membranes and other echogenic tissue interfaces, which results in tissue liquefaction and hypoechoic transformation of tissue in the treatment zone.[26]

CHALLENGES OF ULTRASOUND FOR HISTOTRIPSY

Diagnostic US provides many benefits for real-time histotripsy visualisation as described above. However, intrinsic limitations in the ability to visualise some abdominal tumours with diagnostic US alone can be an important problem when targeting and monitoring histotripsy. While these tumours can be treated with histotripsy, isoechoic or deeply situated tumours, or those that are obscured due to obesity, overlying bowel gas, ribs, or lung, can be difficult to target. Tumours at the liver dome may also be challenging to visualise. US contrast agents may be used to help differentiate tumours from normal surrounding structures, but the safety profile of histotripsy in combination with bubble-containing agents is unknown, and, therefore, this approach is not recommended.

One important difference between conventional diagnostic US and US imaging during histotripsy is the amount of compression possible using each technique. While the diagnostic transducer can be extended to directly contact the abdominal wall, the robotic arm holding the treatment head has a limit to the amount of force that can be applied during scanning and treatment. This results in a limited ability to compress the abdomen to visualize deep or otherwise challenging targets.

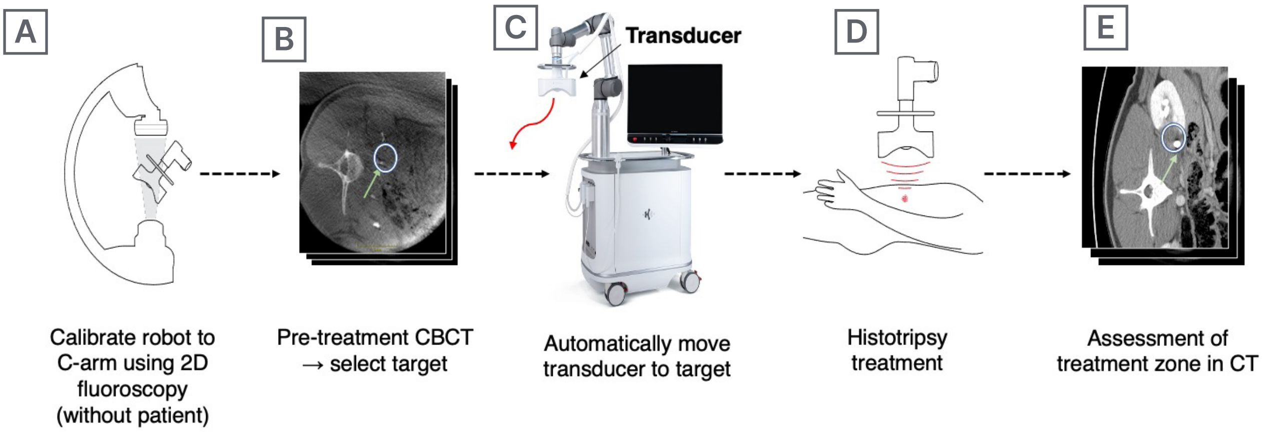
CONE BEAM CT GUIDED HISTOTRIPSY

Cone beam CT (CBCT) offers an alternative or complement to US targeting. The open-bore C-arm architecture of most CBCT systems provides adequate clearance to contain the robotic treatment arm and water bath. The nature of CBCT provides both 2D fluoroscopic images for rapid adjustments and calibration during setup, as well as multi-planar volumetric CT scans for targeting. Unlike US, X-rays can be used to image through air, dense tissue, or depth, allowing for visualisation of targets through bone, lung, and bowel. Iodinated contrast can be safely used to visualise anatomy and differentiate tumours for targeting without adversely affecting histotripsy treatment. CBCT image quality is rapidly improving, but not yet at the level of conventional closed-bore CT scanners. However, the widespread availability, large number of experienced users, and familiar image format will likely aid in the rapid adoption of CBCT guided histotripsy.

Previously proposed CBCT targeting methods leverage the robotic arm for precise positioning of the treatment head based on a target and treatment angle selected on a volumetric CBCT scan (Figure 2).[27] To this end, the spatial relationship between the robotic arm and the C-arm is determined, which is commonly referred to as hand-eye calibration. This can be accomplished during the setup of the system without the patient present by acquiring 2D fluoroscopic or 3D volumetric scans of the transducer head, or a dedicated calibration phantom attached to the robotic arm. These images can be used to determine the 3D position and orientation of the robotic arm attachment in the C-arm co-ordinate space and relate it to the known joint angles of the robotic arm.

After the system is calibrated, the patient is positioned on the table and the water bath fixed over the targeted area. A volumetric 3D scan is taken using the C-arm to capture the target anatomy during compression from the water bath. The physician can select the target in the volumetric scan as well as adjust the orientation of the virtual treatment head, which is displayed in real-time with the volumetric scan. This allows for an opportunity to reduce the number of obstructions along the treatment path

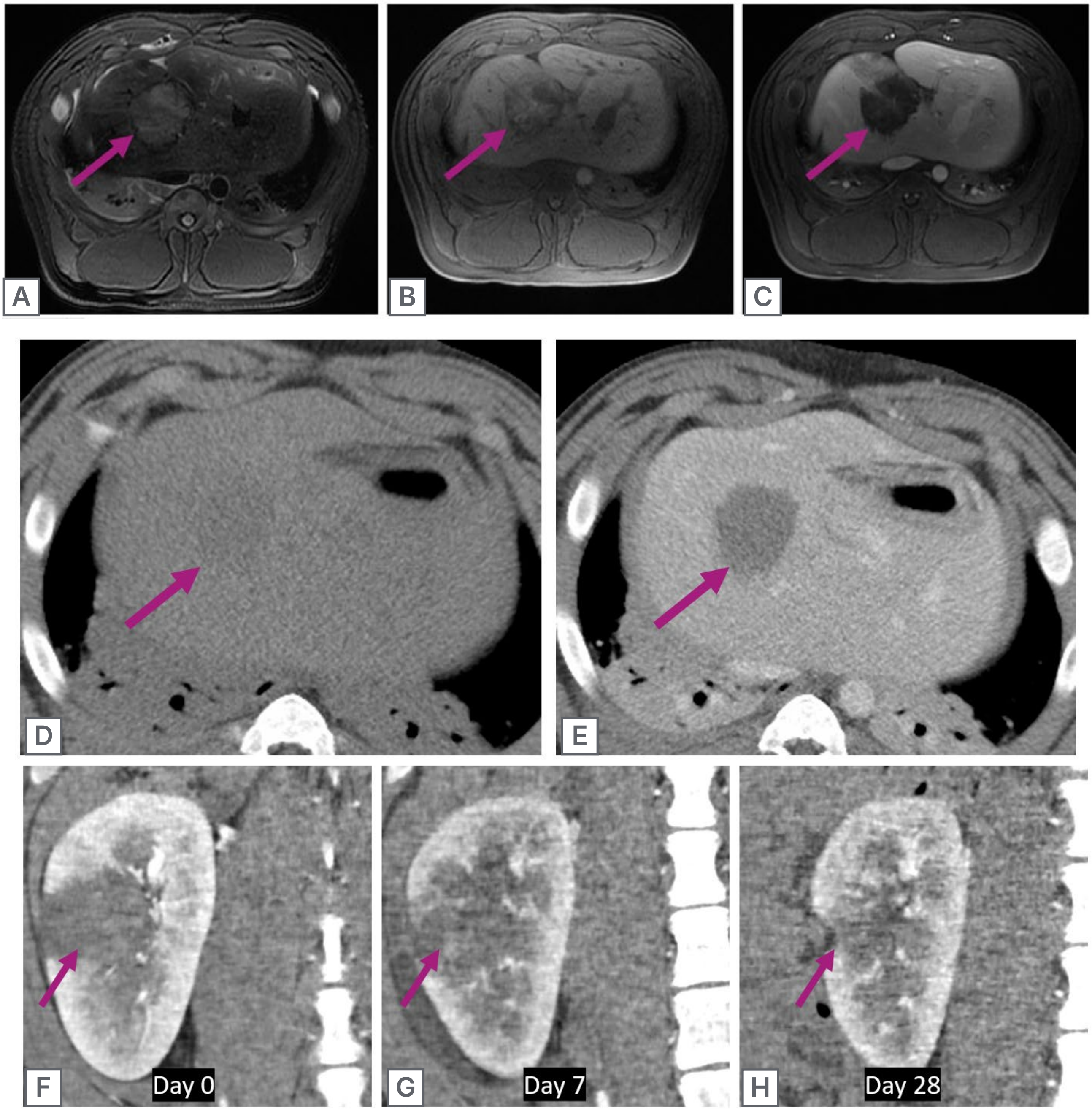
Figure 2: Cone beam CT-guided histotripsy.



To precisely target the kidney and ureter in a healthy swine model, a pre-treatment CBCT was obtained following the administration of IV contrast to opacify the ureter (**B**, green arrow). The treatment zone was selected (**B**, white circle) and the treatment head was automatically moved into position (**C**) to perform the treatment in (**D**). Follow-up CT (**E**) was performed immediately post-procedure with an additional bolus of IV contrast, with the treatment zone (white circle) and undamaged ureter (green arrow) visible.

CBCT: cone beam CT; IV: intravenous.

Figure 3: Post-treatment imaging.



A) Post-treatment T2 weighted MRI following histotripsy treatment in healthy swine liver shows mild hyperintensity of the treatment zone (purple arrow). **B)** T1 weighted MRI. **C)** T1 weighted MRI after IV administration of a gadolinium-based contrast agent. Note the lack of enhancement of the treatment zone.

D) Post-treatment CT shows the difficulty of treatment zone visualisation without IV contrast. **E)** Post-treatment CT after IV administration of iodinated contrast, which demonstrates a well-defined non-enhancing treatment zone with no collateral damage to surrounding liver. This is a typical appearance for post-histotripsy treatments.

F–H) CT imaging of the natural history of a histotripsy treatment in a healthy swine kidney over 28 days (coronal, cortico-medullary phase). Note the rapid and near-complete regression of the treatment zone that may have advantages for diagnosing residual untreated tumour.

IV: intravenous.

and avoid collisions with the patient. After the treatment plan is finalised, the robotic treatment arm automatically moves the histotripsy transducer in position to treat the selected area. The diagnostic US probe mounted inside the treatment head can be used to complement CBCT imaging if the target is visible.

POST-TREATMENT IMAGING

Post-treatment assessment is typically performed with either contrast-enhanced CT or MRI, though contrast-enhanced US may also be used. On B-mode US, the treated area in parenchymal organs (liver, kidney, and spleen) is generally hypoechoic but can be difficult to differentiate from surrounding normal parenchyma. Through the use of contrast-enhanced US, treatment zones demonstrate lack of contrast enhancement, but patent blood vessels are visible traversing the treatment zone.[28] The appearance of treatment zones by CT is well circumscribed, hypoattenuating, and without enhancement after the administration of iodinated contrast materials (Figure 3).[16] By MRI, the treated areas display mild hyperintensity on T1 and T2 weighted imaging, and are similarly non-enhancing after the administration of contrast (Figure 3).[24] Across all imaging modalities, treatment zones appear well circumscribed and precise, closely resembling the prescribed treatment area with minimal or no damage to surrounding tissues. For example, large blood vessels, ureters, and bile ducts are preferentially preserved due to a higher cavitation threshold. Over time, histotripsy treatment zones show rapid resorption (Figure 3) and scar formation within 1–3 months, while maintaining distinct borders from the surrounding parenchyma.[8,14,16]

SUMMARY

Histotripsy is a new focused US treatment modality that destroys targeted tissue through cavitation. US can be used for targeting, cavitation monitoring, and post-treatment assessment due to a co-axially mounted diagnostic transducer contained within the therapeutic transducer. CBCT is being actively explored for histotripsy targeting due to the large open bore, which can contain the therapeutic transducer and coupling water bath, and the ability to visualise structures that may be invisible to diagnostic US. Histotripsy treatment zones are well visualized by CT and MRI and are circumscribed, precise, do not enhance after the administration of intravenous contrast materials, and rapidly resorb, leaving behind small areas of necrosis and scarring.

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Utility of Bedside Lung Ultrasound in the Assessment of Volume Status in Patients on Chronic Haemodialysis

Editor's Pick

My Editor's Pick is an insightful research article exploring different methods for estimating 'dry weight' in patients with end-stage renal disease on haemodialysis. Lung ultrasonography has emerged recently as a non-invasive adjunct to physical examination. This study compares patient assessment with conventional clinical methods and with chest ultrasound.

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Abstract

Aim: The estimation of the 'dry weight' in a patient on haemodialysis with end-stage renal disease is an important clinical challenge to date. Physical examination has its limitations in the precise assessment of volume status. The monitoring of blood volume, natriuretic peptides, and bioimpedance spectroscopy are explored as a guide for the ultrafiltration process during haemodialysis (HD) therapy. Unfortunately, none of these methods has shown promising results when used in isolation and has serious limitations. The point-of-care lung ultrasonography has emerged recently as an adjunct to physical examination as a non-invasive, radiation-free technique to estimate extravascular lung water. In this study, the authors aimed to compare the volume status assessment in end-stage renal disease patients on HD using conventional clinical methods, bio-electrical impedance, and chest ultrasound (US).

Materials and Methods: A prospective cohort study was conducted on 34 patients undergoing regular HD in the Department of Nephrology dialysis centre at the University College of Medical Sciences Guru Teg Bahadur Hospital, Delhi, India, a multi-speciality tertiary care centre. Parameters included to assess the dry weight of patients were bio-impedance spectroscopy and chest US, measured in two phases: 30 minutes before and 10–60 minutes following the HD session.

Results: A total of 100 assessments were done on 34 patients over 6 months. The mean pre-HD extracellular water was 17.52±2.69 L and post-HD was 16.38±2.46 L, showing a significant reduction (<0.001). The bioimpedance analysis showed that 44% of the volume status assessments had fluid overload (≥1.1 L), even when the patients were considered to be in a state of clinical euvolemia, while 79% of the assessments had a Comet Score of ≥3 suggesting a fluid overload state. Most assessments showed a significant reduction in the number of B-lines (i.e., 62% [Comet Score of between 0–2]). The mean post-HD Comet Score was 1.73±1.36 (37%).

Conclusion: Chest US to assess Comet Score is highly correlated with the clinical signs and symptoms. Lung Comet Scores can also be highly correlated with ultrafiltration volume, and thus can be used as a good marker for achieving dry weight in dialysis patients.

Key Points

1. Over- and underestimation of dry weight for a prolonged time has a significant impact on morbidity and mortality in patients on haemodialysis (HD).

2. Chest ultrasound is the most recent method in clinically detecting extravascular lung water and estimating dry weight in patients with end-stage renal disease on HD.

3. The present study added weight to the role of chest ultrasound in lung water measurement in patients on HD, and compared it with body fluid volume status.

INTRODUCTION

Estimation of reliable and reproducible dry weight in patients with end-stage renal disease on haemodialysis (HD) is a clinical challenge to date. 'Dry weight' is the targeted post-HD weight where the patient is as close as possible to their normal hydration state, without having any symptoms indicating over- or under-hydration at or after HD treatment. Clinical estimation of the dry weight in patients is done by a trial-and-error method, correlating it with a history of conditions resulting in extracellular volume overload (increased sodium intake) or depletion (excessive sodium losses in conditions like persistent diarrhoea) and their related symptoms like dyspnoea, postural dizziness, cramps, and headache. Clinical signs such as blood pressure (BP) with postural changes, weight with its interdialytic changes, neck veins congestion, and oedema provide an evaluation of fluid status.[1] However, evaluating patients clinically alone is not accurate enough. This degree of imprecision is reflected in the intradialytic symptoms of chronic volume overload, which results in poor control of BP.[2] Hence, other methods, including biochemical markers (natriuretic peptides such as atrial natriuretic peptide and B-type natriuretic peptide), bioimpedance analysis (BIA), inferior vena cava diameter and its collapsibility, have been developed over time for the better assessment of the accurate fluid status; however, these methods have several shortcomings, such as poor specificity for natriuretic peptides, poor correlation with extravascular lung volume as compared to total body water (BIA and inferior vena cava diameter and collapsibility). Hence, no method is considered a gold standard, and a combination of two or more methods should be used for a more accurate assessment of fluid status.[1]

Overestimation of dry weight for a prolonged period, without any preventive measure, may result in hypertension, left ventricular hypertrophy, and heart failure (HF). On the other hand, underestimation of dry weight is responsible for chronic dehydration, leading to the development of hypotension.[3] Both these complications significantly impact morbidity and mortality in patients on HD. Therefore, it is obvious that using better assessment methods, which are easy to conduct and cost-effective, for determining volume changes during HD is needed.

A lung ultrasonography (USG) is the most recent method being utilised for the detection of extravascular lung water. The US beam is reflected by sub-pleural thickened interlobular septa (a low impedance structure surrounded by air with a high acoustic mismatch) in presence of excessive lung water. This US reflection generates hyperechoic reverberation artefacts between the thickened septa and the overlying pleura known as 'lung comets', or B-lines.[4] Lung comets are defined as vertical artefacts that arise from the pleural line and then extend to the edge of the screen, which moves synchronously with respiration.

The dynamics of B-lines were first evaluated by Noble et al.[5] in patients undergoing HD. They reported a real-time decrease in these artefacts when the volume was removed and suggested the use of this technique in the assessment of euvolemia.[5] Mallamaci et al.[6] further investigated this relationship between lung US findings, status of body fluids volume, and echocardiographic parameters in patients on HD. They found a strong association between the lung US and altered left ventricular functions, but no association with hydration status was assessed by bioimpedance.[6] Trezzi et al.[7] reported a significant correlation between fluid overload before and after HD, and weight loss with the number of B-lines[7].

In this study, the authors aimed to evaluate the feasibility of lung water measurement by chest US in patients on HD and compare the lung water and body fluid volume status, as assessed by a clinical assessment, chest US, and bioimpedance spectroscopy (BIS). The secondary objective of their study was to test the regression of lung comets (B-lines) according to fluid removal in patients on HD.

MATERIAL AND METHODS

This cross-sectional study was conducted at a dialysis centre in the Department of Nephrology at the University College of Medical Sciences Guru Teg Bahadur Hospital, Delhi, India, a multi-speciality tertiary care centre. The sample size was computed as n=34 using the calculation for the proportion of the hospital-based population, with a confidence interval of 95%; an expected prevalence of 40%; a power of 80%; an error of 5%; acceptable absolute and relative precision of 6%; and p=0.05. Written informed consent was taken. All patients received a conventional intermittent 4-hour dialysis, using low permeability polysulfone membranes with a standard bicarbonate dialysate. Prescribed weight was taken from the patient logbook and estimated by the attending nephrologist based on clinical criteria such as weight, BP, and presence of oedema or vascular congestion.

Inclusion and Exclusion Criteria

Inclusion criteria for cases were that the patients were on bi-weekly maintenance HD, were of either gender, and over the age of 18. Patients on once- or thrice-weekly HD; had lung diseases such as pulmonary fibrosis; Stage III and IV of dyspnoea according to the New York Heart Association Functional Classification (NYHA) showing HF, which could affect the results of lung US regardless of the hydration; pacemakers or implantable electronic device; or major amputations of extremities were excluded. A conventional intermittent 4-hour dialysis was given to all patients, using a low permeability polysulfone membrane with a standard bicarbonate dialysate. Data collection was done on a pre-designed proforma. The rate of ultrafiltration was prescribed clinically, based on the interdialytic weight gain in comparison to the targeted weight by the treating nephrologist. Assessment of the weight was done by the attending nephrologist based on clinical criteria like weight, BP, oedema, or vascular congestion, and compared with the prescribed weight taken from the patient logbook. The dry weight assessment parameters, including BIS and chest US were measured twice: 30 minutes before and 10–60 minutes after the HD session.

A gap of at least 1 month was kept in case more than one assessment is done for a single patient.

Informed written consent was taken from all the enrolled participants.

DATA COLLECTION

Data collection was done per the pre-designed proforma blinded to the ultrafiltration rate, as prescribed clinically according to the interdialytic weight gain in comparison with the target weight by the treating nephrologist. This included demographic parameters of the patient; measurements of BP in the supine position after a 10-minute rest using an aneroid sphygmomanometer with documentation of an episode of intradialytic hypotension (systolic BP: <90 mmHg; diastolic BP (DBP): <60mmHg); weight being assessed with an electronic scale, height being assessed with conventional measures, and BMI being calculated using the Quetelet Index (weight [kg]/height [m^2]).

Bioimpedance Analysis

QuadScan 4000 Touch (Bodystat, Douglas, Isle of Man) was used to measure calf BIA. BIS was performed 30 minutes before HD and 10–60 minutes after the HD session by making the patient lie down in bed. The wrist of the contralateral arms of the arteriovenous fistula and the homolateral ankle was used for the placement of electrodes. Fluid overload was defined as the difference between extracellular water (ECW) as measured by BIA pre- and post-dialysis (ECW BIA pre-dialysis-ECW BIA post-dialysis). Requirements before performing BIA included fasting for 4–5 hours the patient was to refrain from any physical exercise a minimum of 12 hours, caffeine (i.e., tea, coffee, and energy drinks), and consumption of alcohol for 24 hours.

Chest Ultrasound

Chest US was performed by the same radiologist, who has over 20 years of experience in chest US. The MicroMaxx® Ultrasound System (Sonosite, Bothell, Washington, USA) with a 6 MHz vascular probe was used for the imaging to look for an alveolar-interstitial syndrome characterised by the presence of specific artefacts called B-lines or 'comet tails'. The presence of comet tails was proof of ling congestion caused by fluid overload in patients on HD.[8] US was performed in the supine position. A longitudinal scan in the left hemithorax (second to the fourth intercostal space) and right hemithorax (second to the fifth intercostal space) at the parasternal, midclavicular, anterior axillary, and midaxillary lines of each side in a total of 28 sectors was performed. Hyperechogenic linear artefacts that were emerging from the pleural line, up from the bottom of the screen, and coherent with respiratory movements were defined as the B-lines. The Comet Score was determined by the total sum of the B-lines found in each examined site, which reflected the extent of extravascular accumulation of the fluid in the lung.

Study Variables

Definitions

Dry weight was defined as the weight estimated by the attending nephrologist and based on clinical criteria such as weight, BP, the presence of oedema, or vascular congestion. The accumulated weight was defined as the subjective dry weight gain, while weight loss was defined as the difference between the pre-and post- dialysis weight changes. Residual weight was defined as the difference between obtained weight after dialysis and the subjective dry weight.

Impedance results

The reference values calculated using impedance for fluid overload to define euvolemia in the normal population were within the range of -1.1 –1.1 L.[9] Patients were considered dehydrated if the fluid volume was less than the reference value (-1.1 L) and euvolemic if the volume of fluid was within the reference range (±1.1 L); they were considered to be in in overload if the fluid volume was greater than the reference value (1.1 L).

Results of lung ultrasound

Pulmonary congestion by fluid overload in patients was defined with the following characteristics:[10] multiple artefacts per scan (minimum three artefacts) and bilateral positivity.

Clinical Outcomes

The average ultrafiltration rate was calculated as follows

$$\text{Ultrafiltration rate (mL/h/kg)} = \frac{\text{(pre-HD weight}-\text{post-HD weight [kg])} \times 1{,}000\ \text{(mL/kg)}}{\text{Session duration (h)} \times \text{post-HD weight (kg)}}$$

Statistical Analysis

Data analysis was done using SPSS Statistics version 21.0 (IBM, Armonk, New York, USA). Categorical variables were presented as numbers and percentages, while continuous variables were presented as mean±standard deviation and median. Quantitative variables were presented using the Student's t-test/Mann–Whitney U test and the qualitative variables were correlated using the χ^2 test. The Pearson correlation coefficient was used to correlate quantitative variables with each other. A p value of <0.05 was considered statistically significant.

RESULTS

This cross-sectional study was conducted over 6 months to determine the efficacy of chest US in the assessment of body fluid volume status in patients with chronic kidney disease (CKD) on dialysis. A total of 100 assessments were done on 34 patients over the 6 months. There were 8 (23%) females and 26 (76%) males for whom chest US and BIS were performed pre- and post-dialysis (Table 1). Most patients (12 [61.7%]) were aged 51–60 years. The mean age of the study population was 54.8 years. The oldest patient was 80 years old. The mean height of the patients was 1.66±0.07 m and BMI 22.66±3.66 kg/m^2. BMI was calculated from the pre-dialysis weight using the Quetelet Index (weight [kg]/height [m^2]). Most of the patients, (24 [70.5%]) had normal body weight (BMI: 18.5–24.9 kg/m^2) and five (14.7%) were underweight (BMI: <18.5 kg/m^2).

Of the authors' patients, 97% had hypertension and 62% had BP readings above 140/90 mmHg. Intradialytic hypotension (BP: <90/60) was found in 3% of the assessments. Diabetes was found in 18 (52%) of the patients, while five (15%) had coronary artery disease and three (9%) had chronic obstructive pulmonary disease. A total of 85% of patients showed no limitation of ordinary physical activity (NYHA Stage I) while 15%

Table 1: Demographics and clinical profile of the studied population.

Study Variables	Values (mean value±SD)
Age (mean±SD)	54.80±11.02
HD duration (months [median, IQR])	8 (3.0–24.0)
HB (g/dL)	7.344±1.470
Albumin (g/dL)	3.012±0.550
Height (m)	1.66±0.07
BMI	22.66±3.66
Pre-dialysis weight (kg)	61.98±10.29
Dry weight (kg)	59.85±10.22
Clinically accumulated weight (kg [patient weight-dry weight])	2.12±1.50
Post-dialysis weight (kg)	59.89±10.18
Residual weight (kg [post-dialysis weight-dry weight])	0.05±0.93
Ultrafiltration (mL)	2,547.00±1,075.24
Urine output (mL)	295 (105–510)

HD: haemodialysis; IQR: interquartile range; SD: standard deviation.

showed restriction of ordinary physical activity (NYHA Stage II).

Table 1 depicts the mean values of the patients' pre-dialysis weight, dry weight, and clinically accumulated weight were 61.98±10.29 kg, 59.85±10.22 kg, and 2.12±1.5 kg, respectively. Post-dialysis weight and residual weight were 59.89±10.18 kg and 0.05±0.93 kg, respectively. Pre-dialysis weight was between 50-70 kg in 76% of the assessments. Dry weight was assessed by trial-and-error methods using various clinical parameters. Figure 1A depicts that the dry weight was between 50–70 kg in 73% of assessments. Clinically accumulated weight was between 1–3 kg in 47% of assessments and 8% of the patient's assessments showed that there was no weight gain seen during the inter-dialysis period. A total of 72% of the assessments had a post-dialysis weight between 50–70 kg. Approximately 53% of assessments showed significant residual weight, while 47% of assessments showed no residual weight.

Figure 1B depicts that the mean pre-HD ECW was 17.52±2.69 L and post-HD was 16.38±2.46 L, showing a significant reduction ($p<0.001$). A total of 44% of the volume status assessments, as per BIA, showed fluid overload (≥1.1 L) even when the patients were considered to be in a state of clinical euvolemia. A total of 79% of the assessments had a Comet Score of ≥3, suggesting a fluid overload state. The mean pre-HD Comet Score was 4.54±2.53. A significant reduction in the number of B-lines was seen with most of the assessments (i.e., 62% had a Comet Score of between 0–2). Figure 1C depicts the mean post-HD Comet Score, which was 1.73±1.36. Of the 100 assessments, 37% had significant B-lines (≥3 per scan) and were considered to be in fluid overload, even after achieving a state of clinical euvolemia.

Figure 2 depicts the correlation between residual weight by clinical methods, fluid overload by BIA, and ultrasonography (USG) chest Comet Score post-dialysis. There was a significant correlation between fluid overload as per BIA and USG chest Comet Score post-HD ($p<0.001$; $r^2=0.75$), while no significant correlation could be seen between residual weight, as assessed by clinical methods and fluid overload as per BIA or USG chest Comet Score post-HD ($p=0.2763$ and 0.1972, respectively; $r^2=$ 0.0056 and 0.0101, respectively).

DISCUSSION

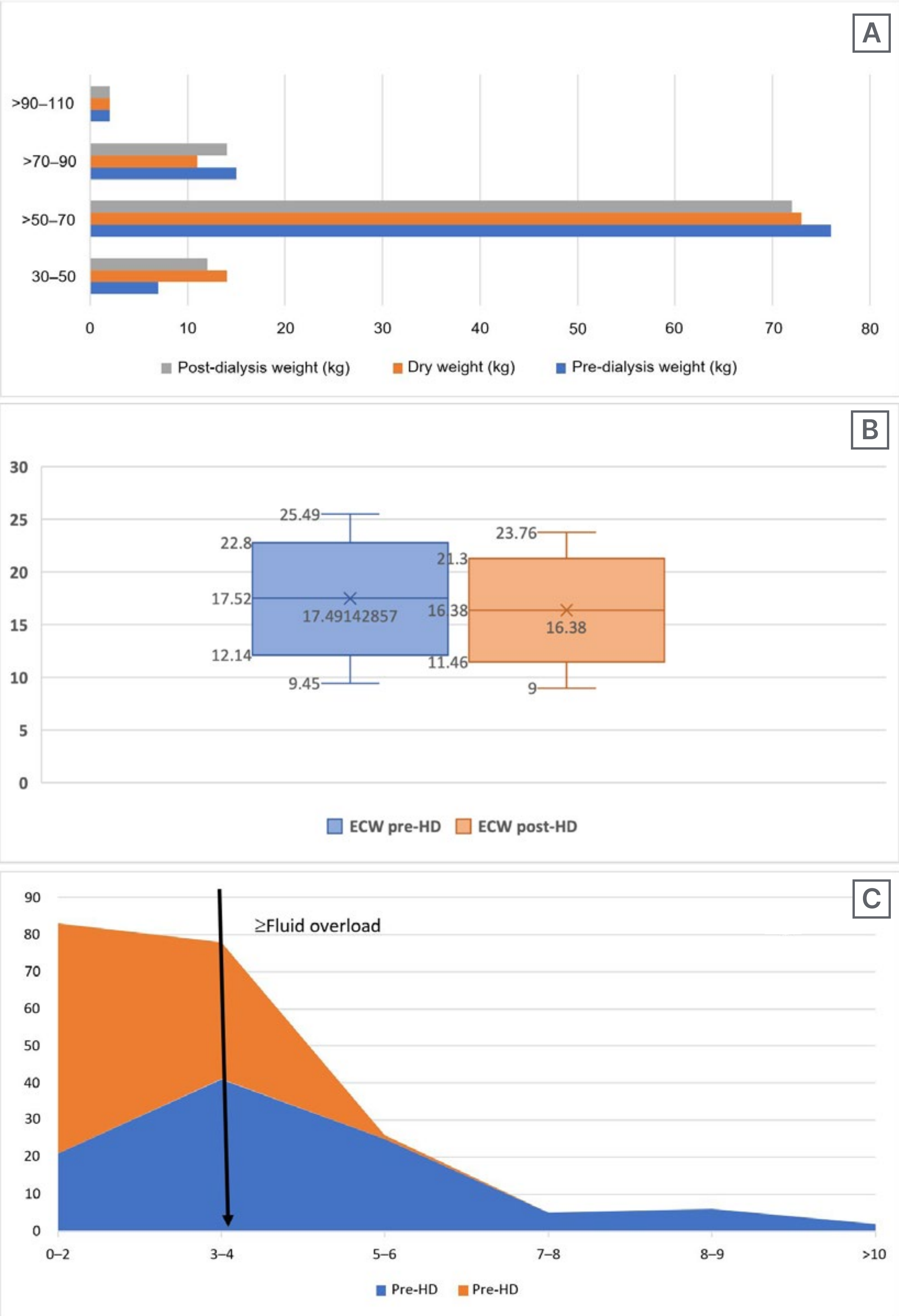
Assessment of reliable and reproducible dry weight in patients on HD is a challenging clinical task. The authors' study aimed to compare the volume status assessment in patients with CKD on HD using conventional clinical methods, bioelectrical impedance, and chest US. A total of 100 assessments were done on 34 patients with CKD and biweekly maintenance HD.

In the authors' study, there was a male predominance (76%). Similarly, studies by Bardai et al.,[3] Torino et al. (65.0%),[11] Vitturi et al. (63.3%),[12] and Allinovi et al.[13] (60.8%) on bedside lung US for volume status assessment in patients on dialysis had a male predominance, with a male:female ratio of 1.1:1.0. Torino et al.[11] in their LUST study found that 65% of the patients were males.

In the authors' study, hypertension was the most common comorbidity seen among patients with CKD (97%), followed by diabetes (52%), coronary artery disease (CAD [15%]), and chronic obstructive pulmonary disease (9%). Similarly, studies by Kuzuhara et al.[14] and Youssef et al.[15] showed that hypertension was the commonest comorbidity seen among patients with CKD, accounting for 41 (83.7%) and 30 (75.0%) cases, respectively. Other studies by Fraser et al.[16] on comorbidity burden in patients with CKD also reported predominance of hypertension (1,528 [87.8%]), followed by diabetes (294 [16.9%]), CAD (398 [22.9%]), and respiratory disease (181 [10.4%]).

In this study, high BP (≥140/90 mmHg) was found in most patients during the pre-dialysis period (i.e., 62% of the assessments). Similarly, a study by Rahman et al.[17] reported high BP in 87.7% of the patients. In another study by Yang et al.[18] on the paediatric population, hypertension was observed in 11 (47.8%) of patients. Recommendations from the *Kidney Disease Outcomes Quality Initiative* (KDOQI) suggest that decreasing fluid overload in the interdialytic period can help in better control of BP in patients on dialysis.[19]

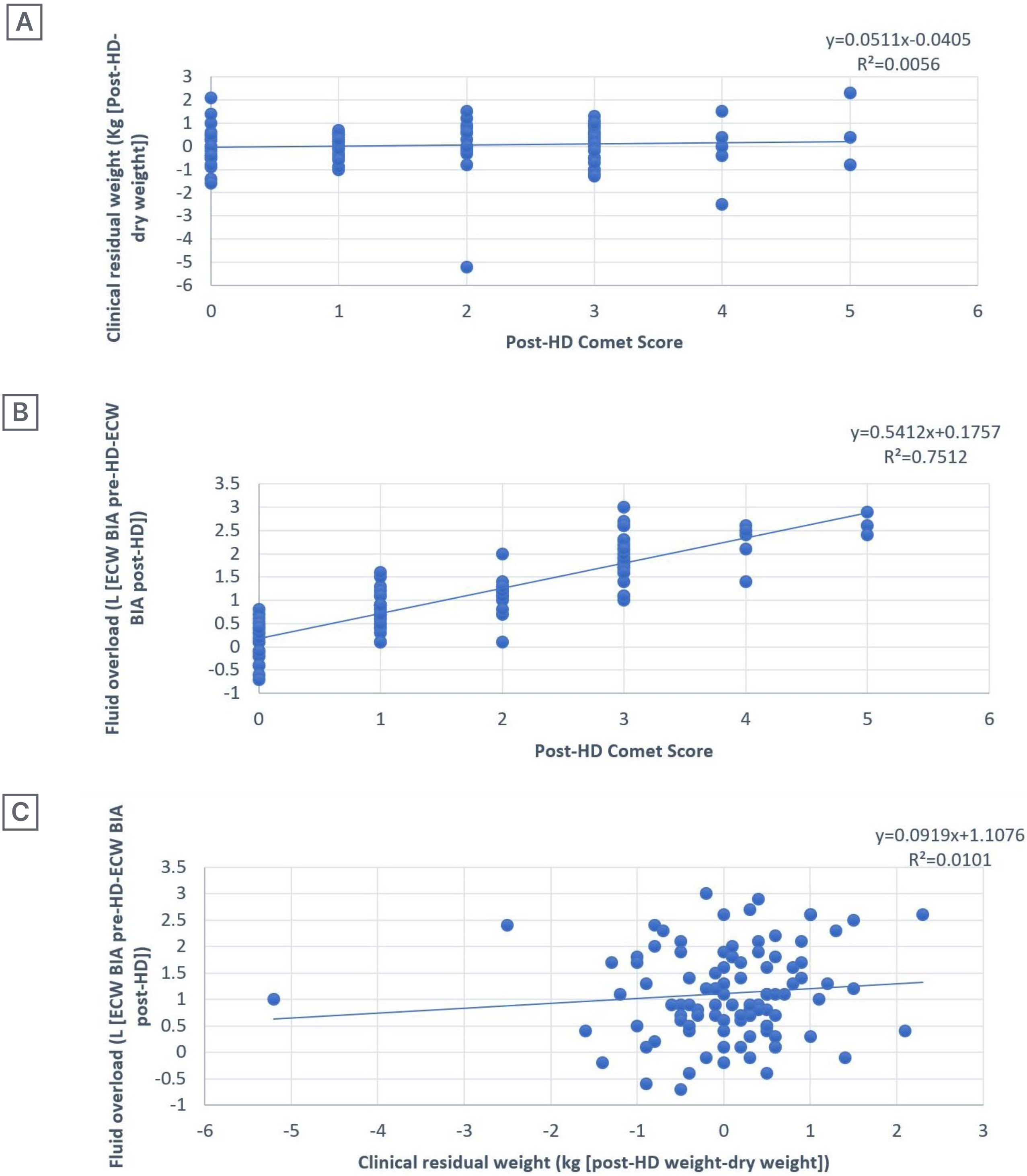
Figure 1: Analyses of patients pre- and post-haemodialysis.



A) Pre- and post-HD and dry weight recordings of patients with CKD. B) Mean ECW measurement on BIA pre- and post-HD. C) Pre- and post-HD Comet Score on chest US.

BIA: bioelectrical impedance analysis; CKD: chronic kidney disease; ECW: extracellular water; HD: haemodialysis; US: ultrasound.

Figure 2: Post-haemodialysis Comet Scores in correlation to clinical residual weight and fluid overload, as well as clinical residual weight and fluid overload.



A) Correlation between post-HD Comet Score (chest USG) and clinical residual weight in kg (post-HD weight-dry weight). **B)** Correlations between post-HD Comet Score (chest USG) and fluid overload (ECW BIA pre-HD-ECW BIA post-HD). C) Correlation between clinical residual weight in kg (post-HD weight¬-dry weight) and fluid overload in L (ECW BIA pre-HD-ECW BIA post-HD).

BIA: bioelectrical impedance analysis; ECW: extracellular water; HD: haemodialysis; USG: ultrasonography.

In the authors' study, intradialytic hypotension (BP: ≤ 90/60 mmHg) was found in three patients. Out of the three patients, two had diabetes and hypertension, while one had underlying CAD. One patient also had a low pre-dialysis BP recording (<90 mmHg). In another study by Sands et al.[20] intradialytic hypotension was found in 17.8% of treatments, with a higher prevalence in patients with diabetes and lower pre-dialysis systolic BP.

In this study, most of the assessments show a pre-dialysis weight between 50–70 kg (76% of patients). The mean pre-dialysis weight was 61.98±10.29 kg, while studies by Raimann et al.[21] and Passauer et al.[22] reported a mean pre-dialysis weight of between 75.70±16.20 kg and 75.00±18.00 kg, respectively. Dry weight in most of the assessments was between 50–70 kg (73%). The mean dry weight was 59.85±10.22 kg. Similarly, Alexiadis et al.[23] found the mean dry weight of patients to be 73.28±16.50 kg in their study; however, in a study on fluid overload in patients on HD, Antlanger et al.[24] found a mean dry weight of between 75.09±19.20 kg.

In the author's study, 47% out of 100 assessments had a clinically accumulated weight of between 1–3 kg (pre-dialysis weight-dry weight). On the other hand, 8% showed no weight gain. The mean clinical accumulated weight was 2.12±1.50 kg. Similarly, Vitturi et al.[12] reported a clinically accumulated weight of between 2.60±1.50 kg.

Patients with greater interdialytic weight gain had higher DBP readings in the authors' study. Similarly, Ipema et al.[25] reported a higher DBP with a higher interdialytic weight gain, which is an independent risk factor for cardiovascular mortality.

In this study, most of the assessments had post-dialysis weights between 50–70 kg (72%). The mean post-dialysis weight was 59.89±10.18 kg. However, the mean post-dialysis weight in a study by Basso et al.[26] and by Maduell et al.[27] was significantly higher (71.40±13.60 kg and 69.50±14.80 kg, respectively).

In the authors' study, the mean residual weight was 0.05±0.93 kg. Similarly, Bardai et al.[3] reported the mean residual weight to be 0.56±1.18 kg in their study. The mean pre-dialysis ECW on BIA in the authors' study was 17.52±2.69 L and 16.38±2.46 L post-HD ($p<0.001$). On the other hand, Papakrivopoulou et al.[28] and Yang et al.[18] reported a mean ECW of between 14.04±0.23 and 7.80±3.40 L pre-dialysis, respectively, and a mean ECW of between 13.21±0.21 and 7.20±3.30 L, respectively. There is a positive correlation between weight loss and percentage reduction in ECW. Patients with higher serum urea, albumin, creatinine, potassium, and normalised protein nitrogen appearance had greater ECW fall on univariate analysis. In context, with other reports of patients with some residual renal function and on diuretics showed smaller changes in ECW.[29]

In the authors' study, 56% of the assessments showed patients to be euvolemic as per BIA, while 44% were hypervolemic (≥1.1 L). Significant fluid overload (≥1.1 L) was associated with higher BP recordings in 32 out of 62 assessments.

Similarly, Bardai et al.[3] found that 38% of the patients were in a fluid overload state as per BIA, post-dialysis. Wizemann et al.,[30] in their study on risks of overhydration in patients with CKD, found that an overhydrated state is an independent predictor of hypertension and, therefore, mortality on long-term dialysis is second only to diabetes.

The mean pre-HD Comet Score in the authors' study was 4.54±2.53, while the post-HD Comet Score was 1.73±1.36 ($p<0.0001$). Similar findings were reported by Vitturi et al.,[12] with a mean pre- and post-HD Comet Score of between 3.13±3.40 and 1.41±2.47, respectively.

In this study, 23% of assessments had significant lung congestion in the post-dialysis period, even when patients were considered to have clinical euvolemia. Similar results were seen in a study by Bardai et al.,[3] where 20% of the patients had significant lung congestion post-dialysis. On the contrary Basso et al.,[26] found that 15 (65%) of the patients had significant pulmonary congestion after dialysis. The exclusion of patients having severe dyspnoea (NYHA Stages III–IV) was the cause of the lower Comet Scores in the authors' study, while relatively higher Comet Scores in other studies was secondary to patients having decompensated HF. Depending on the pathologic conditions, there will be differences in the density and distribution of BIA. Thickened subpleural interlobular septa are represented by the dispersed septal syndrome. Alveolar flooding, also known as an interstitial-alveolar syndrome and white lung, is a more severe variant of interstitial lung disease.[31] Gas exchange is compromised, and the dyspnoea gets worse in the later stages. According to the NYHA's functional classification, the relationship between the Comet Score and the degree of dyspnoea makes logical sense.

The authors' study was cross-sectional, and the sample size is not large enough to give results that may be representative of the general population. Device validity was not confirmed using the tracer dilution technique.

CONCLUSION

Chest US performed at the bedside is now emerging as a reliable, easy-to-apply, and safe method for measuring lung water and intravascular overload and their reduction after dialysis, even in asymptomatic patients. Comet Score, assessed on chest USG, is highly correlated with the clinical signs and symptoms; it even precedes the development of symptoms in patients on HD. Moreover, lung Comet Score is also highly correlated with ultrafiltration volume and thus, can be used as a good marker for achieving dry weight in patients on dialysis. These observations strongly support the use of lung US in estimating volume overload and monitoring the response to therapy in patients on HD. Furthermore, the authors' findings also conclude that the lung US Comet Score is superior to clinical methods in assessing the volume status in patients on HD and, hence, the target dry weight for these patients.

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Correlation Between Neutrophil-Lymphocyte Ratio, Platelets-Lymphocyte Ratio, and High-Resolution CT in Patients with COVID-19

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Abstract

Background: COVID-19 is a highly infectious disease that necessitates simple and rapid methods for recognising severe patients.

Aims: To correlate between chest lesions in CT, neutrophil-lymphocyte ratio (NLR), and platelets-lymphocytes ratio in patients with COVID-19, and to detect their cut-off values as an early warning of severe COVID-19 in Egyptian patients.

Subjects and Methods: A cross-sectional study included 100 adult patients with COVID-19 attending Ahmed Maher Teaching Hospital, Cairo, Egypt. Clinical, laboratory, and radiological assessments were done. They were classified according to their CT grades into three groups: seven patients with a normal chest CT, 45 non-severe cases, and 48 severe cases.

Results: Dyspnoea was the most common symptom among the severe cases (79.2%) and fever among non-severe cases (71.1%), while cough (85.7%) was the most common among cases with a normal CT. The age, NLR, C-reactive protein (CRP), and D-dimer of severe cases were significantly the highest, while the absolute lymphocytes were significantly the lowest. Highly significant positive correlations were found between CT grades with D-dimer, NLR, and CRP; significant positive correlation was found with age; and significant negative correlation with CT. Using receiver operating characteristic analysis, areas under the curve of D-dimer, NLR, age, CRP, ferritin, and platelet-lymphocyte ratio were 0.760, 0.698, 0.640, 0.627, 0.614, and 0.595, respectively. The optimal cut-off value of NLR was 2.50 with 0.74 specificity, 0.61 sensitivity, and 67.5 accuracy.

Conclusion: NLR is a reliable and easy-to-use predictor of COVID-19 severity. NLR (>2.5) should prompt prescription of a chest CT as it could reveal essential lesions that influence further management.

Key Points

1. COVID-19 is an abruptly progressing and sometimes lethal contagious disease, which necessitates simple and rapid methods for recognising patients with severe responses.

2. Circulating biomarkers are potentially useful in the diagnosis and prognosis of patients with COVID-19. The neutrophil-lymphocyte ratio is an easy-to-use and reliable predictor in the effective screening, early isolation, and management of patients infected with COVID-19.

3. A neutrophil-lymphocyte ratio more than 2.5 should persuade clinicians to define chest CT, as it could manifest primary lesions that could impact further management.

INTRODUCTION

COVID-19 is an abruptly progressing and sometimes lethal contagious disease. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was first reported in Wuhan, China, at the end of 2019. The World Health Organization (WHO) announced it as a pandemic in March 2020.[1]

Circulating biomarkers are potentially helpful in the diagnosis and prognosis of patients with COVID-19.[2] Disturbance of erythrocyte sedimentation rate and C-reactive protein (CRP) were connected to increased severity of COVID-19 infection.[3] There are also some eminent changes in haematological parameters such as leucopenia, lymphopenia, elevated lactate dehydrogenase, D-dimers, and ferritin, that may be specific for SARS-CoV-2 infection.[4]

The platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte ratio (NLR) are considered as indices of systematic inflammatory reaction.[5] They have been vastly evaluated in many other conditions such as malignancies, cardiovascular diseases, and intra-cerebral haemorrhage. Greater values were connected to intense forms of diseases with very bad prognosis.[6] As they are one of the routine laboratory tests, they are non-costly, available, and easily measurable.[7] NLR can be utilised as a prompt warning indicator of severe COVID-19.[8] However, most previous studies were reported from China and, to a lesser extent, some countries in Europe, without concern for PLR.

Imaging studies play a significant function in the diagnosis and follow-up of patients with COVID-19. A CT of the chest is used as the main imaging tool in doubtful cases and is a valuable tool for supervising the changes and reflecting the severity during treatment.[9] Abnormal findings in CT can be present even in asymptomatic patients; therefore, combining imaging assessment with clinical and laboratory results could favour precocious diagnosis of COVID-19.[10]

The severity of lung involvement on high resolution CT correlates positively with laboratory findings, and this provides an insight into the appropriate interval of chest CT to reduce radiation exposure and support proper management of patients with COVID-19.[11]

The purpose of this study was to correlate between PLR and NLR the degree of severity of CT lesions in patients suffering from COVID-19, and to detect cut-off values for these ratios to be used as an early warning indicator for determining the severity of COVID-19 in Egyptian patients.

PATIENTS AND METHODS

Patients

This was a cross-sectional study that included 100 adult patients who attended Ahmed Maher Teaching Hospital, Cairo, Egypt, during the period from March 2020 to April 2021, with symptoms of the clinical characteristics of COVID-19 and confirmed by real-time PCR (RT-PCR). The enrolled patients included 44 males and 56 females with a range of age from 19–88 years.

The protocol was approved by the ethical committee of the General Organization for Teaching Hospitals and Institutes (GOTHI; institutional review board number: HAM00152). Adult patients aged ≥18 years old, having clinical manifestations that included fever and pulmonary symptoms (such as cough, shortness of breath, and chest pain) and who tested positive for SARS-CoV-2 using RT-PCR from respiratory samples (nasal/oropharyngeal swab) were enrolled in the study. Patients with suspected bacterial pneumonia (confirmed by sputum culture), who had an incomplete chest CT examination, were excluded from the study.

Methods

After taking a valid informed consent, clinical, laboratory, and radiological assessments were obtained.

Clinical assessment

A detailed history was obtained and, following a thorough clinical examination, the need for intensive care unit (ICU) admission was recorded. The patients were categorised during an emergency room assessment into two groups according to their O_2 saturation. The normal range of O_2 saturation at rest was defined as 94–98% in patients without chronic lung disease, and between 88–92% in those with chronic lung disease associated with hypoxia.[12] A pulse oximeter reading of 92% or lower was one defining feature of severe condition in acute COVID-19, while a reading of 93–94% indicated moderate severity.[13]

Laboratory assessments

Venous blood samples were sent to assess the following: complete blood count (haemoglobin [Hb] norm: 11.5–15.5 mg/dL; red blood cell [RBC] norm: 4–5.2 ×10^{12}/L; haematocrit norm: 36–45%; absolute lymphocyte norm: 1,000–4,800 /μL; platelets norm: 150,000–450,000 /μL): CRP norm: <5 mg/L; ferritin norm: 10–120 ng/mL; and D-dimer norm: <0.5 μg/mL). NLR and PLR were calculated with the reference values of significance; NLR>2.8 and PLR>180.[2] NLR was calculated using the simple formula: absolute number of neutrophils/absolute number of lymphocytes; and PLR was calculated using the simple formula: absolute number of platelets/ absolute number of lymphocytes.

Radiological assessment

The severity of COVID-19 was categorised on the basis of a chest CT. High resolution CT of the chest was performed using GE64 row 128-slice CT scanning equipment (GE HANGWEI Medical System, Beijing, China).

In all cases, the CT severity scoring system suggested by Pan et al.[14] was calculated for each of the five lobes regarding the extent of pathologic involvement, as follows: 0: no involvement (normal); 1: <5%, mild involvement; 2: 5–25%, mild-to-moderate involvement; 3: 26–50%: moderate involvement; 4: 51–75%, moderate-to-severe involvement; and 5: >75%, severe involvement.

STATISTICAL ANALYSIS

The patients' data were analysed utilising Statistical Package for Social Sciences (SPSS, Windows Version 18, SPSS Inc., Chicago, Illinois, USA). Normality of data was tested using the Kolmogorov–Smirnov test. Most of the variables such as O_2 on admission, NLR, PLR, CRP, ferritin, and D-dimer, were not normally distributed. Therefore, the non-parametric tests were used. $P<0.05$ was considered statistically significant.

Continuous variables were presented as means and standard deviations, while categorical variables were outlined as numbers and percentages in each category. The Kruskal–Wallis test was applied to compare between more than two groups, while categorical variables were compared using chi-square test. Receiver operating characteristic curve (ROC) was used to assess the optimal cut-off value of the continuous NLR, its sensitivity, specificity, accuracy, and positive and negative predictive values (PPV and NPV). True-positive cases were those with high NLR and high CT chest grades and true-negative cases were those with low NLR and low chest CT grades, while false-positive cases were those with high NLR and low chest CT grades and false-negative cases were those with low NLR and high chest CT grades.

Sensitivity was measured using the equation: true-positives/(true-positives plus false-negatives); while specificity was measured as true negatives/(true-negatives plus false-positives). PPV was defined as the percentage of cases with high CT chest grades that had high PLR. NPV was defined as the percentage of cases with low CT chest grades that had low PLR. Maximal accuracy and PPV/NPV closest to 1 were used for determining cut-off level.

RESULTS

The clinical characteristics of the participating subjects are shown in (Table 1). Insignificant differences were observed in terms of sex, presence of associated chronic diseases, and clinical symptoms. Most of them exhibited

Table 1: Clinical characteristics of the study sample according to CT chest groups (chi square test).

	Total (N=100)		Severe (N=48)		Non-severe (N=45)		Normal CT (N=7)		p
	N	%	N	%	N	%	N	%	
Sex									
Males	44	44.0	22	45.8	18	40.0	4	57.1	0.655
Females	56	56.0	26	54.2	27	60.0	3	42.9	
Comorbidities									
Diabetes	42	42.0	19	39.6	21	46.7	2	28.6	0.590
Hypertension	30	30.0	12	25.0	16	35.6	2	28.6	0.538
Ischaemic heart disease	8	8.0	3	6.2	5	11.1	0	0.0	0.384
Heart failure	1	1.0	N/A	N/A	1	2.2	0	0.0	0.447
Pulmonary diseases (restrictive/obstructive)	7	7.0	3	6.2	4	8.9	0	0.0	0.525
Chronic hepatic diseases	0	0.0	0	0.0	0	0	0	0.0	N/A
Chronic renal diseases	6	6.0	1	2.1	5	11.1	0	0.0	0.118
Symptoms and signs									
Fever	65	65.0	29	60.4	32	71.1	4	57.1	0.465
Cough	54	54.0	28	58.3	20	44.4	6	85.7	0.081
Sore throat	26	26.0	15	31.2	9	20.0	2	28.6	0.457
Dyspnoea	72	72.0	38	79.2	31	68.9	3	42.9	0.105
Chest pain	28	28.0	13	27.1	13	28.9	2	28.6	0.980
Need for ICU during hospital stay	12	12.0	7	14.6	5	11.1	0	0.0	0.348

ICU: intensive care unit; N/A: not applicable.

comorbidities such as diabetes (42%), followed by hypertension (30%), while the minority was suffering from ischaemic heart disease (8%), pulmonary diseases (7%), chronic kidney disease (6%), and heart failure (1%). Nobody was suffering from chronic liver disease.

Depending on their chest CT, patients were classified into three groups: seven patients (four males and three females) with a normal chest CT; 45 (18 males and 27 females) were non-severe (score 1–3); and 48 (22 males and 26 females) were severe cases (score 4–5). The most common symptoms were dyspnoea (72%), fever (65%), and cough (54%), followed by chest pain (28%) and sore throat (26%). Only 12% were admitted to ICU during their hospital stay. Dyspnoea was the most common symptom among severe cases (79.2%), fever was the most common among non-severe cases (71.1%), while cough was most common among patients with a normal CT (85.7%).

Table 2 reveals highly significant differences between the the groups of cases for NLR (p=0.002), CRP (p=0.005), and D-dimer (p=0.004); and significant differences for age (p=0.039) and absolute lymphocytes (p=0.030). Age for the severe cases ranged from 19.00–88.00 years old, with a mean age of 57.35±15.71 years old. Mean age for non-severe cases was 54.69±11.87 years old, ranging from 23.00–77.00 years old, while the mean age for patients with a normal chest CT was 42.57+12.66 years.

Table 2 : Baseline characteristics of the laboratory investigations of the study sample according to CT chest groups (Kruskal–Wallis Test).

	Total (N=100)		Severe (N=48)		Non-severe (N=45)		Normal (N=7)		p
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age	55.12	14.25	57.35	15.71	54.69	11.87	42.57	12.66	0.039*
O_2 on admission	92.91	6.01	92.60	5.96	92.69	6.23	96.43	4.31	0.066
Hb (11.5–15.5 mg/dL)	12.19	2.11	11.95	2.01	12.21	2.19	13.76	1.78	0.129
RBC (4.0–5.2 $\times 10^{12}$/L)	4.56	0.83	4.48	0.92	4.58	0.76	4.89	0.62	0.338
HCT (36–45%)	36.76	6.49	35.64	6.43	37.18	6.48	41.41	5.13	0.074
Absolute lymphocyte (1,000-4,800 /μL)	1.58	0.78	1.48	0.74	1.54	0.71	2.51	0.92	0.030*
NLR (<2.8)	4.77	4.40	6.05	5.05	3.95	3.44	1.24	0.77	0.002†
Platelets (150,000–450,000 /μL)	253.66	92.90	250.35	98.52	253.09	89.89	280.00	78.81	0.590
PLR (<180)	206.35	140.09	216.90	152.86	207.91	132.05	124.06	64.23	0.058
CRP (<5 mg/L)	49.51	76.36	66.85	95.58	38.71	53.72	4.56	5.83	0.005†
Ferritin (10–120 ng/mL)	486.90	578.80	473.60	458.55	554.09	698.03	163.72	144.54	0.308
D-dimer (<0.5 μg/mL)	0.57	0.61	0.80	0.79	0.39	0.21	0.22	0.02	0.004†

The test result variable(s): age, platelet/lymphocyte ratio (>180), C-Reactive protein (<5 mg/L), D-dimer (<0.5 μg/mL) have at least one tie between positive and negative actual state groups. Statistics may be biased.

*p>0.05: significant difference

†p>0.01: highly significant difference

CRP: C-reactive protein; Hb: haemoglobin; HCT: haematocrit; NLR: neutrophil-lymphocyte ratio; PLR: platelets-lymphocyte ratio; RBC: red blood cell.

The age, NLR, CRP, and D-dimer of severe patients were significantly the highest, while the absolute lymphocytes were significantly lower than those of non-severe cases and cases with normal chest CT. Among the severe cases, PLR was insignificantly the highest, while O_2 on admission, Hb, RBC count, haematocrit, and platelets were insignificantly lower than the other two groups.

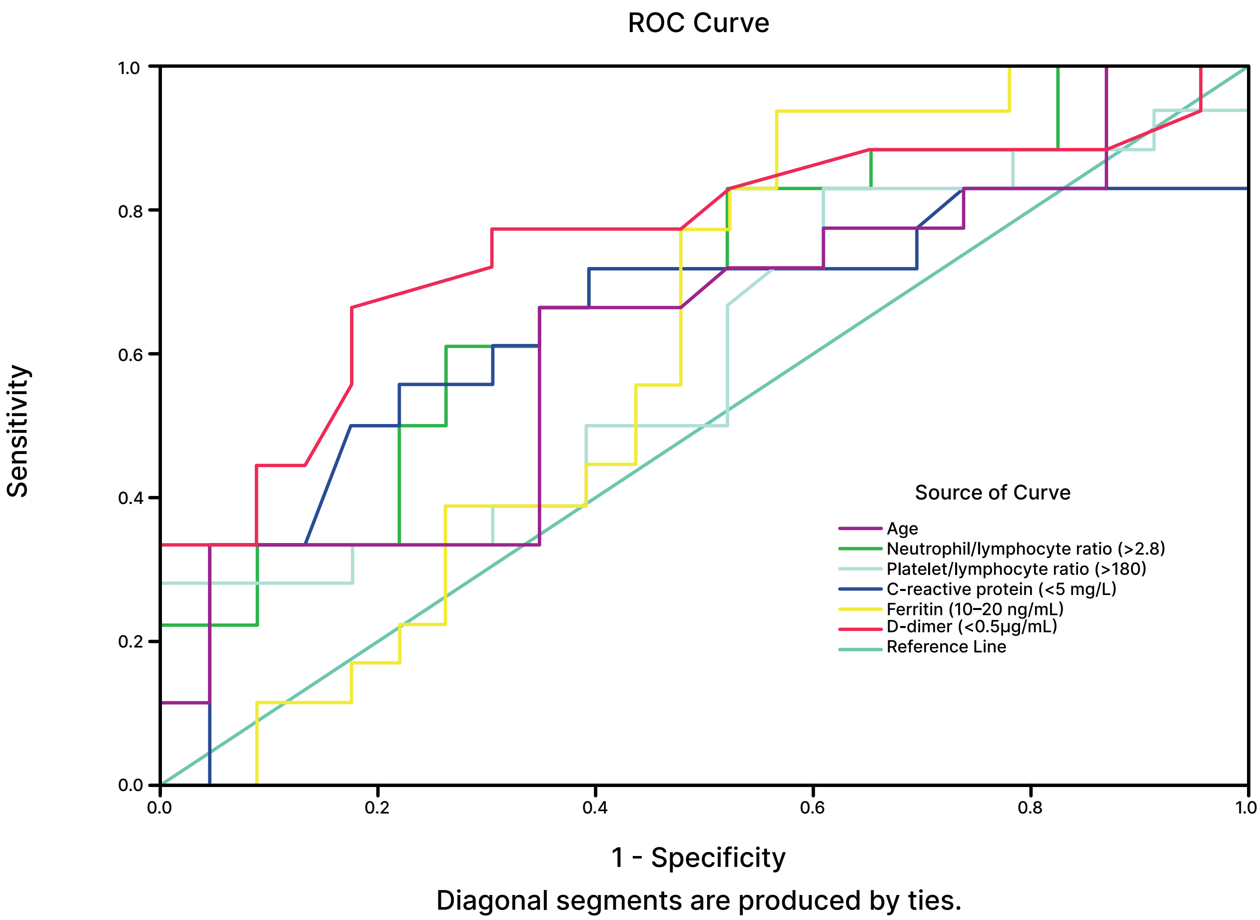
Using the ROC analysis (Figure 1), areas under the curve (AUC) of D-dimer, NLR, age, CRP, ferritin, and PLR were 0.760, 0.698, 0.640, 0.627, 0.614, and 0.595, respectively. They are useful prospective diagnostic biomarkers for subsequent studies because its AUC was more than 0.5000.

The most appropriate cut-off value for NLR was 2.50, with 0.74 specificity, 0.61 sensitivity, 0.70 PPV, 0.66 NPV, 1.07 PPV/NPV, and 67.50 accuracy (Table 3).

DISCUSSION

Being a highly infectious disease, COVID-19 depletes effective health care facilities. Circulating inflammatory biomarkers used to evaluate immune status are helpful in the diagnosis of COVID-19. Inflammation has a remarkable role in the progress of viral pneumonia, and severity of the inflammation relates to the adaptive immune system.[2] Rapid, simple, and available risk stratification methods are obligatory to distinguish with severe disease.[15]

Figure 1: Using receiver operating characteristic curve analysis, areas under the curve of D-dimer, neutrophil-lymphocyte ratio, age, C-reactive protein, ferritin and platelets-lymphocyte.



ROC: receiver operating characteristic.

Table 3: Neutrophil-lymphocyte ratio cut-off levels determining the COVID-19 CT chest progression using receiver operating characteristic analysis.

Positive if greater than or equal To	Sensitivity	Specificity	PPV	NPV	Accuracy	PPV/NPV
1.1	0.944	0.17	0.53	0.76	55.90	0.70
1.2	0.889	0.22	0.53	0.66	55.30	0.80
1.3	0.889	0.26	0.55	0.70	57.50	0.78
1.4	0.833	0.39	0.58	0.70	61.20	0.82
1.6	0.833	0.44	0.60	0.72	63.40	0.82
1.8	0.833	0.48	0.61	0.74	65.55	0.83
1.9	0.778	0.48	0.60	0.68	62.80	0.88
2.0	0.667	0.52	0.58	0.61	59.45	0.95
2.1	0.667	0.57	0.61	0.63	61.60	0.96
2.2	0.667	0.61	0.63	0.65	63.80	0.98
2.4	0.667	0.65	0.66	0.66	65.95	0.99
2.5	0.611	0.74	0.70	0.66	67.50	1.07
2.6	0.556	0.74	0.68	0.62	64.75	1.09
2.8	0.500	0.74	0.66	0.60	61.95	1.10

NPV: negative predictive values; PPV: positive predictive values.

There are some changes in blood such as leucopenia, lymphopenia, and disturbance of CRP and erythrocyte sedimentation rate, which are correlated to severity of COVID-19 infection. Some are discriminatory for SARS-CoV-2 infection, including D-dimer, lactate dehydrogenase, and ferritin.[4]

This study encompasses easily available investigations such as a complete blood picture to find the effect of COVID-19 in the respiratory system and its probable progress by comparing with the same radiological severity, thus helping to determine early measures of treatment. Enrolled patients were classified according to CT into three groups; cases with normal CT chest, non-severe cases (mild, mild-to-moderate, and moderate), and severe cases (moderat-to-severe and severe).

In this study, 100 adult patients (44 males and 56 females) clinically suspected to have COVID-19 were assured by positive result of RT-PCR. Male to female ratio was 22:26 in severe cases, 18:27 in non-severe cases, and 4:3 in cases with normal CT, with insignificant differences observed in terms of sex.

Yang et al.[5] in China found that in a total of 93 patients, the male to female ratio was 56:37; with 18:6 in severe and 38:31 in non-severe cases. Furthermore, Fu et al.[16] in Suzhou, China, found that in a total of 75 patients, the male to female ratio was 35:24 in non-severe cases and 10:6 in severe cases. Similar to the authors' findings, both have found no statistical difference as well.

In this study, there was a significant difference for age ($p=0.039$). Mean age for severe cases was 57.35 ± 15.71, 54.69 ± 11.87 years for non-severe cases, and 42.57 ± 12.66 years for cases with a normal chest CT. Similarly, Yang et al.[5] found a significant difference for age. They determined the mean age as 58 years, with the maximum as 83 years. The mean age of non-severe patients was 42 years. The age of severe cases was significantly higher than non-severe cases. However, Fu et al.[16] found an insignificant difference for age, where mean age among severe cases was 51.8±12.8 years and 45.1±14.0 years for non-severe cases.

In this study, insignificant differences were observed in terms of clinical symptoms. The most common symptoms were dyspnoea (72%), fever (65%), cough (54%), chest pain (28%), and sore throat (26%). Dyspnoea was the most common symptoms among the severe cases (79.2%), fever was the most common among non-severe cases (71.1%), while cough was most common (85.7%) among the cases with normal CT. In accordance with the results of this study, Yang et al.[5] detected fever (83.8%) and cough (67.7%) as the initial and most common symptoms. Furthermore, Fu et al.[16] found the most common symptoms to be fever (62; 86.7%), cough (54; 72%) and sore throat (12; 16%).

This study showed that most of the patients exhibited comorbidities such as diabetes (42%), hypertension (30%), ischaemic heart disease (8%), pulmonary disease (7%), chronic kidney disease (6%), and heart failure (1%).

Liu et al.[17] in China assumed that the most common comorbidity in their study was hypertension (19.0%), followed by coronary heart disease (9.5%). Yang et al.[5] found that severe individuals were associated with hypertension (66.8%), diabetes (54.2%), heart failure (37.5%), and renal failure (33.3%). In agreement with the results of this study, all these studies agreed that diabetes and hypertension are among the most common comorbidities reported in severe cases.

According to National Institutes of Health (NIH) guidelines, published in 2021,[18] COVID-19 has been categorised clinically into asymptomatic, mild, moderate, severe, and critical, taking into consideration the peripheral O_2 saturation and CT severity. In agreement, the authors' study postulates that, among the severe cases, O_2 on admission was insignificantly lower than the other two groups.

Shi et al.[10] in Wuhan, China, postulated that chest CTs in COVID-19 manifest as bilateral, ground-glass opacities with ill-defined margins located sub-pleuraly. CT lesions can be present even in asymptomatic patients, but can rapidly progress into a diffuse ground-glass opacity or consolidation pattern within 1–3 weeks. Kumar et al.[19] in India suggested that patients with comorbidities have more pulmonary involvement than patients with no non-comorbidities, which indicates the rapid progression of pulmonary damage in groups with comorbidities. Depending on the CT chest examination in the authors' study, patients were classified into three groups: seven patients (3 males and 4 females) with normal chest CT, 45 patients (18 males and 27 females) with non-severe cases (mild, mild-to-moderate, and moderate), and 48 patients (22 males and 26 females) with severe (moderate-to-severe and severe) cases.

It has been noticed that in severe cases, the absolute values of lymphocytes decreases rapidly while the white blood cell count increases gradually, leading to deflection between the absolute value of neutrophils and lymphocytes, which gave the idea that NLR may be correlated with the poor prognosis of COVID-19. NLR is also associated with bad prognosis in other diseases such as pancreatic cancer and sepsis.[20]

Our study revealed highly significant differences between the three groups of cases in NLR (p=0.002), CRP (p=0.005) and D-dimer (p=0.004), and significant differences in absolute lymphocytes (p=0.03). NLR, CRP, and D-dimer of patients with severe disease were significantly higher. Among the severe cases, PLR was insignificantly the highest, while Hb, RBCs, haematocrit, and platelets were insignificantly the lowest. Spearman’s correlations between CT grades and laboratory investigations revealed highly significant positive correlations with D-dimer, NLR and CRP.

These results were coincident with those of Yang et al.,[5] who proved that elevated NLR was a distinct biomarker of prognosis of COVID-19. These findings were proportionate with other studies on the relation between NLR and prognosis of other infectious diseases.[21]

In this study, ROC analysis using AUC for D-dimer, NLR, CRP, ferritin, and PLR were

0.760, 0.698, 0.640, 0.627, 0.614, and 0.595, respectively. They could be used as prospective diagnostic biomarkers because their AUC are more than 0.500.

Sarkar et al.[22] in India postulated that prognostic value of NLR can be used for early recognition of progressing cases. NLR ≥5 identifies patients likely to develop severe COVID-19, while NLR ≥6 identifies patients with high risk of mortality. Man et al.[2] in Romania also found that both NLR and PLR correlate with chest CT grades. When the NLR value is below 5.04 and CT score is less than 3, the probability of CT changes is 94%; meanwhile if the NLR is higher than 5.04, the probability of CT changes is only 50%. Additionally, Yang et al.[5] postulated that a threshold at 3.3 for NLR has showed a high possibility of deterioration from mild to severe, with high sensitivity and specificity, and Liu et al.[17] have demonstrated that subjects with elevated NLRs (≥4.87) were as much as 8.5 times (95% confidence: 1.962–36.471) more prone to deteriorate than those with a low NLR (<4.87).

In accordance with these results, the authors reported the optimal cut-off value for NLR as 2.50 with specificity of 0.74, sensitivity of 0.61, PPV of 0.70, NPV of 0.66, PPV/NPV of 1.07, and accuracy of 67.5. Therefore, NLR is recommended as a simple tool to estimate the severity of COVID-19 and to assess the prognosis, but this is not applicable for PLR. Fu et al.[16] have also found that the blood indices had more AUC than inflammatory markers (NLR: 0.88; D-dimer: 0.74; fibrinogen: 0.74; and lymphocyte: 0.72; versus CRP: 0.72; and procalcitonin: 0.67).

In the authors' study, only 12% of patients were admitted to ICU during their hospital stay, while among 351 patients who were enrolled by Hashem et al.[15] in Egypt, 145 (41.3%) were admitted to ICU. They suggested the most appropriate cut-off point for NLR to predict severe COVID-19 with ICU admission as more than eight, with 60.7% sensitivity and 85.9% specificity. They also reported that the value for PLR of more than 192 has 74.5% sensitivity and of 60.2% specificity. Their high cut-off point may be due to the fact that all patients included were severe cases admitted to ICU.

A major limitation of this study is the lack of a control group.

CONCLUSION

The NLR is an easy-to-use and reliable predictor in the effective screening, early isolation, and early management of patients with COVID-19, but PLR is not reliable. A value of 2.5 for NLR seems to be suggestive for COVID-19 deterioration. NLR of more than >2.5 should persuade clinicians to prescribe a chest CT as it could manifest primary lesions that would impact further management.

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