Physical and Engineering Sciences in Medicine (2021) 44:347–350
https://doi.org/10.1007/s13246-021-01010-5

TOPICAL DEBATE

In the future, ultrasound guidance in radiotherapy will become a clinical standard

Emma Harris[1] · Davide Fontanarosa[2,3] · Clive Baldock[4]

Published online: 17 May 2021

Introduction and overview: Clive Baldock, moderator

In modern radiotherapy, imaging is an important component in the treatment process where it is used for planning the doses to be delivered and for verifying and monitoring the position of the target during treatments. Recent developments in imaging have contributed to advancing radiotherapy techniques' such as image-guided radiotherapy (IGRT) for intrafraction motion management and adaptive radiation therapy (ART). This is has resulted in the ability to deliver highly conformal radiation doses with increased precision, which has enabled the safe increase in the dose that can be delivered to the tumour, resulting in improvements in clinical outcomes and the implementation of hypofractionated radiotherapy regimens.

Although x-ray imaging has predominantly been used in radiotherapy for many years, more complex radiotherapy such as ART, demands an imaging modality with greater soft tissue contrast so radiotherapy targets can be imaged directly. A requirement that has led to the recent introduction of the MR-linac [1]. Ultrasound also offers soft tissue contrast and may have advantages in terms of imaging rates, we therefore considered it pertinent to consider the role of ultrasound imaging in future radiotherapy treatments.

In this timely debate, Emma Harris and Davide Fontanarosa discuss whether ultrasound guidance in radiotherapy will become a clinical standard in the future.[1]

Dr. Emma Harris is a Reader of Imaging and Radiation Physics at the Institute of Cancer Research in London, UK. Her research focuses on the application of radiation physics, ultrasound physics engineering and image processing to improve radiotherapy. She has spent more than a decade leading experimental studies of image guided radiotherapy and has devised and conducted a number of clinical studies investigating the use of ultrasound for image guidance of radiotherapy of cervical cancer, prostate cancer and paediatric cancers.

Dr. Davide Fontanarosa was awarded his PhD in Medical Physics from the University of Maastricht (the Netherlands) with a thesis on: "Evaluation of speed of sound aberration and correction for ultrasound guided radiation therapy". Presently, he works as Associate Professor in the School of Clinical Sciences at the Queensland University of Technology (Brisbane, Australia). Previously he worked as Senior Scientist at Maastro Clinic (Maastricht, the Netherlands) and at Philips Research (Eindhoven, the Netherlands). His major fields of research are: artificial intelligence for automatic interpretation of ultrasound imaging; image guidance in radiotherapy; minimally invasive surgery and orthopaedics (in particular using quantitative ultrasound imaging); advanced radiotherapy treatment planning and adaptation strategies. Associate Professor Fontanarosa is currently supervising seventeen PhD students; he is the Unit coordinator for the Honours students in five different disciplines cross faculty and he teaches Physics of Ultrasound in the Physics of Medical Imaging Unit. He is the inventor of 9 patents, and authored 80 peer reviewed publications, one book and 6 book chapters.

✉ Clive Baldock
cbaldock@uow.edu.au

1 Division of Radiotherapy and Imaging, The Institute of Cancer Research, London, UK

2 School of Clinical Sciences, Queensland University of Technology, Brisbane, Australia

3 Centre for Biomedical Technologies, Queensland University of Technology, Brisbane, QLD 4000, Australia

4 Research and Innovation Division, University of Wollongong, Wollongong, NSW 2522, Australia

[1] Contributors to Topical Debates are selected for their knowledge and expertise. Their position for or against a proposition may or may not reflect their personal opinions.

EMMA HARRIS

DAVIDE FONTANAROSA

For the proposition: Emma Harris

Opening statement

Adaptive radiotherapy, both on a fraction-to-fraction basis and during radiation delivery, i.e., intrafraction motion compensation, is gaining traction as the safest way to deliver radiation dose, particularly in the context of dose escalation or hypofractionated treatments [2]. A requirement of daily adaptive radiotherapy is direct visualisation of soft tissues and for intrafraction motion compensation we ideally require sampling rates that minimise the time and space over which we predict motion. Ultrasound can meet these requirements, it can directly image soft tissues and is the only imaging modality currently used in radiotherapy that can perform real-time (> 20 Hz) volumetric imaging. Importantly, it can also be integrated with any treatment machine, including robotic linacs and particle therapy machines.

There is already a clinical standard for ultrasound guided prostate radiotherapy. In some centres it is routinely used to directly image the prostate to assess interfraction motion and centres are using it to directly monitor prostate motion during radiation therapy. We have shown it is highly accurate for this purpose [3] and it is the only commercial solution that does not require implanted markers and/or frequent x-ray imaging [4]. Pioneering studies of ultrasound guidance of liver and cervix radiotherapy have demonstrated the utility of ultrasound an adaptive radiotherapy setting [5, 6].

Ultrasound is one of the most widely used medical imaging technologies, its use increased tenfold between 2000 and 2011, which would not be the case if it was not capable of exquisite image quality [7]. I argue that we have yet to appreciate the full advantage of modern ultrasound in radiotherapy because of the practical barriers imposed by its current implementation. The use of a hand-held "torch-light" type probe used in diagnostics is simply not suitable for the radiotherapy clinic. For starters, the user cannot remain in the room! New innovations in probe technology such as flexible transducers, wearable probes [8] and capacitive micromachined transducers [9] made from low atomic number material are far more suited to the radiotherapy environment. User dependence is already being tackled in the diagnostic setting with the use of machine learning to automate image interpretation and registration. Significant advances in artefact reduction have been implemented on the state-of-the-art commercial ultrasound machines. In addition, there is a significant body of work on the use of machine learning algorithms to help guide the ultrasound user [10]. Such algorithms can also be used for autonomous systems, medical robot control has gained wider acceptance over the past decade, and robots are now assisting in the field of ultrasound guided surgery. With these innovations, ultrasound guidance in radiotherapy can be redesigned from the ground up to overcome the practical barriers of the past, enabling it to be used a clinical standard for adaptive radiotherapy. Finally, ultrasound is attractive for proton beam therapy of paediatric patients, not only does its non-ionising and real-time nature allow for safe and continuous monitoring of tissue motion, ionacoustics continues to show promise for the verification of the proton Bragg peak.

Against the proposition: Davide Fontanarosa

Opening statement

After many years working in the field of ultrasound based guidance, in particular in radiation therapy, I have come to the conclusion that ultrasound imaging is an extremely powerful modality, but difficult to introduce in standard clinical practice. It is complex to interpret and so it requires a long training which is typically not part of the standard training of clinicians in radiotherapy. This does not make it appealing for institutions which need to plan and support training for multiple personnel to cover for possible leaves and resignations. Moreover, one-button systems such as cone beam CT for example are much easier and faster to integrate in the workflow.

Radiotherapy is historically a technology driven field, and ultrasound is not a technology which the vendors can find economically interesting to invest on, because the potential revenue is limited. Especially if compared against the direct competitors, such as for example the MR-LINAC. The big players in the field have invested substantial amounts of money in the development of these systems, which are also definitely more impactful, marketing-wise, for hospitals. Typically, the installation of one of these systems always makes the news, while the same is usually not true for cheaper ultrasound systems. For this and other reasons, these systems currently are not actively developed anymore by any major vendor in this space and, considering the long timeframes needed to bring medical technology to the clinic, in my opinion this can be considered a clear sign of what a realistic future scenario will be. Meanwhile, (conventional) radiotherapy is possibly evolving towards different future treatment paradigms, less local, less ablative, more systemic. So it seems unlikely that, on the prospective time scales within which accurate geometric control of ablative treatments is necessary, any new ultrasound guided system will become standard of care.

To bridge the gap between its undisputable scientific and clinical relevance and its "marketing appeal", the solution is automation. Nowadays artificial intelligence can help perform several interpretation and use tasks automatically [11], thus partially or even totally removing the need for expert operators. But we are still far from having all the tools available to make the workflow competitive against one-button-click systems. Increasingly more companies are proposing artificial intelligence applications together with their ultrasound systems [12], but mainly for diagnostic or operator guidance purposes. In radiotherapy specific problems connected with the presence of radiation during treatment need to be solved, and presently there is no autonomous or semi-autonomous system for ultrasound imaging in these conditions. Some solutions have been proposed in literature involving robotic arms [13], but only as support for trained and skilled operators. Intelligent autonomous robotic systems would be the ideal solution [14], but they would require extensive development investments and, once more, significant time frames, which do not seem to be part of any big players' plans currently. Moreover, robots are particularly complicated to introduce into standard clinical workflows because of safety concerns and because of efficiency limitations.

For the proposition: Emma Harris

Rebuttal statement

Ultrasound images, like most medical images, are difficult to interpret for those that have not received training. It is true that within the radiotherapy clinic, radiographers/therapists have typically had little exposure to ultrasound, however, that does not mean this challenge cannot be overcome such that staff are fully competent and the service is maintained. And there are precedents for this, for example, the team at Bristol University Hospitals, one of the busiest centres in the UK, have described their successful roll out of the Elekta Clarity Prostate Ultrasound System which has now been clinical for over 5 years and have treated in excess of 300 patients with Clarity ultrasound guidance and they adopted ultrasound monitoring during prostate radiotherapy back in 2017 [15, 16]. Furthermore, CBCT, although widely established, is not a one-button system, soft tissue verification requires training and expertise. In the context of adaptive radiotherapy, local experience of the implementation of plan of the day for radiotherapy for cervical cancer using CBCT is not straight-forward and, similar to the introduction of ultrasound, requires sophisticated radiographer-led training programmes.

Whilst vendor investment in ultrasound-guided radiotherapy has slowed, it has not completely ground to a halt. Elekta is actively supporting research into ultrasound-guided radiotherapy and General Electric Healthcare are engaged in a significant programme of work with the University of Wisconsin developing an MRI compatible 4D ultrasound probe for use in ultrasound-guided liver radiotherapy [17]. Whilst ultrasound systems, may not command the same headlines as the MRI integrated devices, it is likely that most radiotherapy service will continue to be delivered by C-arms linacs, and as such these should be subject continued development and optimisation using add-ons such as real-time imaging systems. Clearly, with reference to the aforementioned research development, this will still include ultrasound. Furthermore, radiotherapy is most effective for localised treatments, and whilst there is emerging evidence of an additional, perhaps more systemic role for radiation when coupled with immunotherapies, the priority remains to detect cancer early and therefore localised radiotherapy will continue to play a role in cancer treatment, and possibly this role will increase further as diagnostics improve. Precise imaging systems will still be required, and arguable precision will need to be increased if we detect smaller tumours, that may be subject to intrafraction motion. A task that I argue is highly suited to ultrasound motion monitoring.

Against the proposition: Davide Fontanarosa

Rebuttal statement

Most of the arguments presented in favour of the proposition are valid in the diagnostic/radiological space, but application to quantitative use for guidance requires significant further efforts. Redesigning all the aspects of an imaging modality, as suggested, is an incredibly complex task. Unfortunately, presently none of this seems to be in the agenda of any of the vendors in this space. Even in literature examples of such applications are still anecdotal (for example, [18]) and with systems far from the high refresh rate which is required to claim real time volumetric imaging. Even if such systems were available, integration with treatment machines is not seamless: the presence of the ultrasound system needs to be taken into account, which very likely means changes in the treatment planning system, in the treatment workflow and in risk management, at the very least. These are all characteristics which do not apply to simple add-on devices.

Prostate is indeed the only organ which is currently clinically supported, several other regions have been investigated over the past decade or more, but they have never resulted in any concrete product. Except for breast [19] for which Resonant Medical (now Elekta) had proposed a separate module, but it has soon been discontinued, for reasons not dissimilar from the ones listed here.

Automation as mentioned is a possible solution to some of these problems. But automating ultrasound image acquisition and interpretation is complicated, much more than other modalities, due to its inherent complexity in imaging borders/interfaces, a problem which has been very poorly discussed and analyzed in literature, especially for quantitative applications [20]. Moreover, machine learning training is typically very sensitive to the field of view (and hence the probe position), as opposed to what happens with other modalities for which more general trainings can be considered, since they always have a reasonably similar way to show the structures.

References

1. Baldock C, Karger CP, Zaidi H (2020) Gel dosimetry provides the optimal end-to-end quality assurance dosimetry for MR-linacs. Med Phys 47(8):3259–3262
2. Keall P, Poulsen P, Booth JT (2019) See, think, and act: real-time adaptive radiotherapy. Semin Radiat Oncol 29(3):228–235
3. Grimwood A, McNair HA, O'Shea TP et al (2018) In vivo validation of Elekta's clarity autoscan for ultrasound-based intrafraction motion estimation of the prostate during radiation therapy. Int J Radiat Oncol Biol Phys 102(4):912–921
4. Bertholet J, Knopf A, Eiben B et al (2019) Real-time intrafraction motion monitoring in external beam radiotherapy. Phys Med Biol 64(15):15TR01
5. Boda-Heggemann J, Sihono DSK, Streb L et al (2019) Ultrasound-based repositioning and real-time monitoring for abdominal SBRT in DIBH. Physica Med 65:46–52
6. Mason SA, White IM, O'Shea T et al (2019) Combined ultrasound and cone beam CT improves target segmentation for image guided radiation therapy in uterine cervix cancer. Int J Radiat Oncol Biol Phys 104(3):685–693
7. Klibanov AL, Hossack JA (2015) Ultrasound in radiology: from anatomic, functional, molecular imaging to drug delivery and image-guided therapy. Investig Radiol 50(9):657–670
8. Bourbakis N, Tsakalakis M (2020) A 3D ultrasound wearable array prognosis system with advanced imaging capabilities. IEEE Trans Ultrason Ferroelectr Freq Control 68(4):1062–1072
9. Salim MS, Abd Malek MF, Heng RB et al (2012) Capacitive micromachined ultrasonic transducers: technology and application. J Med Ultrasound 20(1):8–31
10. Akkus Z, Cai J, Boonrod A et al (2019) A survey of deep-learning applications in ultrasound: artificial intelligence-powered ultrasound for improving clinical workflow. J Am Coll Radiol 16(9):1318–1328
11. Liu S, Wang Y, Lei B et al (2019) Deep learning in medical ultrasound analysis: a review. Engineering 5(2):261–275
12. Gibson LE, Low SA, Bittner EA (2020) Ultrasound teleguidance to reduce healthcare worker exposure to coronavirus disease 2019. Crit Care Explor 2(6):e0146
13. Sandoval J, Laribi MA, Zeghloul S et al (2020) Cobot with prismatic compliant joint intended for Doppler sonography. Robotics 9(1):14
14. Wu L, Jaiprakash A, Pandey AK et al (2020) Robotic and image-guided knee arthroscopy. In: Abedin-Nasab MH (ed) Handbook of robotic and image-guided surgery. Elsevier, London, pp 493–514
15. Hilman S, Smith R, Masson S et al (2017) Implementation of a daily transperineal ultrasound system as image-guided radiotherapy for prostate cancer. Clin Oncol 29(1):e49
16. Richardson AK, Jacobs P (2017) Intrafraction monitoring of prostate motion during radiotherapy using the Clarity® Autoscan Transperineal Ultrasound (TPUS) system. Radiography 23(4):310–313
17. Lee W, Chan H, Chan P et al (2017) A magnetic resonance compatible E4D ultrasound probe for motion management of radiation therapy. IEEE Netw. Sep 2017
18. Camps SM, Costa M, Steven E et al (2017) Evaluation of optical localization in the visible band for ultrasound guidance in radiotherapy using a robotic arm. J Cancer Control Treat 30(5):319–329
19. Berrang TS, Truong PT, Popescu C et al (2009) 3D ultrasound can contribute to planning CT to define the target for partial breast radiotherapy. Int J Radiat Oncol Biol Phys 73(2):375–383
20. Antico M, Sasazawa F, Takeda Y et al (2020) Bayesian CNN for segmentation uncertainty inference on 4D ultrasound images of the femoral cartilage for guidance in robotic knee arthroscopy. IEEE Access 8:223961–223975