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Imaging in interventional oncology, the better you see, the better you treat

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Introduction

The better we see, the better we treat. Radiological imaging has travelled from being a screening diagnostic tool to become part of the image guidance for complex procedures to deliver high-precision healthcare. Interventional radiology and specifically interventional oncology use radiological images to plan, guide and follow patients' treatments. Knowing what each image modality offers is of ample importance to give the spatial and morphological information required to select the most appropriate and accurate assistance for interventional

Summary

Imaging and image processing is the fundamental pillar of interventional oncology in which diagnostic, procedure planning, treatment and follow-up are sustained. Knowing all the possibilities that the different image modalities can offer is capital to select the most appropriate and accurate guidance for interventional procedures. Despite there is a wide variability in physicians preferences and availability of the different image modalities to guide interventional procedures, it is important to recognize the advantages and limitations for each of them. In this review, we aim to provide an overview of the most frequently used image guidance modalities for interventional procedures and its typical and future applications including angiography, computed tomography (CT) and spectral CT, magnetic resonance imaging, Ultrasound and the use of hybrid systems. Finally, we resume the possible role of artificial intelligence related to image in patient selection, treatment and follow-up.

Key words: ablation; embolization; image guidance; radioembolization.

procedures. From percutaneous to endovascular interventions, interventional oncology always needs to balance and take into consideration image quality and radiation dose for the patient and the interventional radiologist. Classically, loss of image quality has been pondered over real time monitoring and radiation dose reduction.¹ Despite currently, with the improvement of ultrasound (US) protocols and tools, new low-dose image algorithms, the use of stereotactic image guidance and robotic systems for endovascular procedures or the wider availability of magnetic resonance imaging (MRI) guidance, this problem has improved in many scenarios, it is

still capital for the physicians to keep in mind and being aware of the necessity for radiation dose reduction in patients. In this review, we will discuss the different image modalities that are more frequently used for oncological procedures, their main indications, advantages and weaknesses to provide a general idea of its current use, their optimal indication and their future in the era of artificial intelligence.

US and US-multimodality fusion

Ultrasound is a widely-available and versatile imaging tool for many interventional oncology procedures. Relative low-cost and real-time imaging capability without ionizing radiation are some of its advantages over other multiplanar imaging modalities. Ultrasound alone or in conjunction with other imaging modalities is invaluable in thermal ablation procedures for pre-procedural planning, intra-procedural guidance, monitoring and assessment of ablation zone. Some authors have reported that total treatment duration might be shorter using ultrasound guidance compared to computed tomography (CT) in easily accessible lesions, but it has not yet been clearly demonstrated.^{2,3} Contrast-enhanced ultrasound (CEUS) as compared to conventional ultrasound has shown to provide better tissue differentiation and improves the detection of tumour lesions compared to conventional ultrasound in different cancer types.^{4,5} CEUS has been investigated for immediate and follow-up imaging of residual disease after percutaneous thermal ablation.⁶ Ultrasound elastography is a non-invasive method for measuring elastic properties of tissue and has been studied in interventional oncology. Preliminary results indicate potential clinical use of ultrasound elastography for ablation monitoring, but future research is warranted to evaluate reproducibility and other elastography methods, establish threshold value and further refine the clinical application.^{7,8} Emerging fusion methods enable synchronized display of real-time ultrasound images with previous CT, MRI or PET as the reference imaging modality, while continuously adapting to ultrasound transducer motion. The variety of fusion methods offers an opportunity when availability of CT or MRI for interventional guidance is limited.^{9,10} Ultrasound fusion combines previously mentioned advantages of ultrasound with superior contrast resolution of multiplanar imaging modalities. The use of ultrasound fusion during interventional oncology procedures aids the identification of lesions and assessment of tumour ablation margins to increase technical success. In case of poor conspicuity of lesion on conventional ultrasound or CEUS, ultrasound fusion with CT/MRI improved lesion detection with reported rate up to 96%.¹¹ Last, US fusion has been reported to yield improved visibility of lesions in the liver or kidney for ablation and can be potentially used to assess the ablation margin.¹²⁻¹⁴

Angiography and CBCT

Angiography and digital subtraction angiography (DSA) are the standard imaging techniques for the evaluation of vascular conditions. A clear understanding of the sometimes complex anatomy and pathology is essential in guiding decision-making during interventional oncologic procedures. As procedures increase in complexity and the therapeutic options require more precise planning and control, the need for better imaging and visualization became obvious. The introduction of C-arm Cone Beam CT technology, which was a more space- and cost-efficient alternative to hybrid rooms in which a conventional CT is used.^{15,16} The basic principle of CBCT is the acquisition of multiple X-ray projections during gantry rotation around a volume of interest. The resulting series of images are back-projected to produce a volumetric dataset. The technology has been evolving ever since with rapid improvement in detector, rotation speeds and software applications. Manufacturers offer different CBCT acquisition protocols targeted and optimized for specific clinical tasks, differing mainly in various trade-offs, such as speed of acquisition, resolution and radiation dose.^{17,18} Since the introduction of CBCT, it was quickly recognized as giving essential additional information for the evaluation of the target lesions and surrounding soft tissue, which led to its routine adoption.¹⁵ CBCT systems allow for high-quality 3D imaging and advanced processing in the IR room, enabling complex procedures in a single modality room, such as combined embolization and ablation.¹⁶ High-quality imaging delivers additional information for more precise decision-making during interventional oncology procedures. CBCT can be used to detect enhancing tumours and tumour feeders, guide tumour targeting in embolization and helps prevent non-target embolization. Additionally, navigation and simulation software can improve the targeting during a procedure where the integration between systems makes it possible to have the navigation overlaying during live fluoroscopy for guidance. Another advantage is that tumour coverage can be assessed directly after the treatment, as with TACE or ablation.¹⁹ Besides all the benefits, there are some limitations to this acquisition, such as limited 3D reconstruction field of view, limited contrast resolution, slower spin rates and higher sensitivity to various artefacts compared to CT imaging.¹⁵⁻¹⁷

Dynamic contrast-enhanced and dual-energy CT in oncologic imaging

Conventional single-energy contrast-enhanced CT gives inherent tissue attenuation and iodine uptake in one static image. Dynamic contrast CT and dual-energy CT (DECT) provide more information, which can be beneficial for oncological patients.²⁰⁻²² Perfusion CT can improve the detection and differentiation of malignant liver lesions, especially HCC, pancreatic lesions and

kidney lesions can be more easily discriminated from benign lesions and normal parenchyma. Evaluation of response to therapy (systemic, intra-arterial and ablative) in liver lesions, pulmonary cancer, pancreatic cancer, GIST, kidney tumours and lymphoma appears to be possible.^{21,23–27} Retrospective data show that perfusion CT could improve the pretreatment prediction of response to radioembolization in HCC²⁸ and is the best predictor of response in colorectal liver metastasis.^{29,30} Moreover, it has shown to be very useful for the early detection of viable tumour after ablation, in which dual-input-deconvolution-mode appears to be the most feasible model.¹⁹ While single energy cannot differentiate between different body materials that have an overlapping linear attenuation coefficient, dual energy can improve material differentiation using two different X-ray energy spectra, from these data, virtual unenhanced images can be extracted and quantification of contrast medium uptake can be done. Tissue can be characterized and subsequently monitored for any changes during treatment. Contrast enhancement is a relatively subjective evaluation of tumour response, with DECT this is made objective, without the need to increase the radiation dose and with the possibility to decrease the contrast dose.³¹ Quantification of tumour burden and boundaries helps in tumour detection, tumour staging, treatment planning and response evaluation.^{22,31,32} A dynamic contrast scan can deliver more information about the pathological tissue, but inherently adds a higher radiation dose.²¹ However, not all possible benefits of DECT and perfusion CT have been proven by research and validation and standardization is needed. Dual-energy CT, especially in the liver, bowel, kidney, pancreas and skin (melanoma) is beneficial because of the easier detection of small hyper- or hypovascularized lesions. Evaluation of the ablation margins and response or recurrence of disease during and after ablation or other targeted therapies is another interesting topic for DECT.^{31–35} Dual-energy CT may allow for better pre-therapy planning due to the identification of vessels than perfusion CT³⁶ and can easily detect the amount of lipiodol deposit in TACE.³⁷ Both perfusion CT and dual-energy CT can make detection of HCC lesions easier, although dual-energy CT provides the same results when scanning in late arterial and portal venous phase, with extra information due to the dual-energy scan and with a lower radiation dose.³⁸

CT and hybrid systems

In 1992, the first hybrid Angio-CT system was developed at the Aichi Cancer Center, in Japan, consisting of two independent systems, an interventional angiographic unit with a sliding tabletop in combination with a fixed CT at the head of the table facilitating patient movement between the two systems without the risk of catheter or needle dislodgement.³⁹ The early systems were mainly utilized for the treatment of HCC, showing improved

detection of small HCC's by CT Hepatic Arteriography (CTHA)/hepatic artery and CT arterial portography (CTAP)/superior mesenteric artery compared to diagnostic CT or MRI with intravenous contrast^{40,41} and higher survival for HCC treated by TACE with Angio-CT compared with a conventional angiography system.⁴² Takada *et al.* reported the usefulness of intra-arterial CT aortography, a sensitive rapid technique for the detection of common and unusual extra-hepatic HCC feeders, preventing time-consuming individual catheterization of suspected feeders followed by DSA and CBCT or contrast-enhanced CT⁴² and Van Tilborg *et al.*⁴³ described an adapted CT hepatic arteriography technique for image guidance during percutaneous liver ablation of recurrences of colorectal metastases with 20 ml contrast through a catheter in the common hepatic artery proximal to the gastroduodenal artery, allowing visualization of a pure arterial phase after 6 s and a mixed late arterial/early portovenous phase after 22 s, enabling repeated contrast-enhanced imaging with minimal amounts of contrast to distinguish recurring or residual tumour tissue from scar tissue.⁴⁴ Furthermore, a retrospective comparative study by the same group reported improved local disease control and 2-year local tumour progression-free survival with transcatheter CT hepatic arteriography-guided ablation compared with conventional CT fluoroscopy, because of increased tumour, needle and ablation zone visualization, with comparable survival and complication rates.⁴⁵ Catheter dislodgement occurs in 5% of patients due to patient movement between angiography room and CT room making a hybrid Angio-CT system a way to prevent this and lead to reduction in procedure time and improved operational utilization of rooms. Although the introduction of the Cone Beam CT (CBCT) has led to marked improvement in visual guidance for interventional procedures, Angio-CT enables larger field of view (FOV) with increased scanning of the whole liver, less respiratory motion artefacts because of faster scanning, less streaking artefacts, higher contrast resolution and better tumour and feeder vessel identification.^{45,46} Angio-CT also permits real-time CT-fluoroscopic guidance, improving precise needle placement in ablation and making nearby critical structures visible during needle placement in complex ablations. In combination with CTHA it is possible to ablate lesions that are not visible by ultrasound or non-contrast CT.⁴⁷ There have been fears for increased radiation exposure due to the Angio-CT, but evidence therefore is lacking. Piron *et al.* found a significant decrease in patient radiation exposure while performing TACE on Angio-CT compared to CBCT.^{48–50} Finally, for certain treatments and lesions (mainly those easily differing from the surrounding tissue) Angio-CT systems have also shown operational efficiency and cost-effectiveness^{51,52} and represent an excellent opportunity to expand the indications that interventional radiologist can perform in the oncology setting.^{53–55}

MRI-guided interventions

In oncology, MRI has positioned itself as a powerful non-invasive diagnostic tool with a solidified position in prostate, breast and liver cancer. Moreover, there is a growing body of literature that discusses the use of MRI as a powerful interventional technique for targeted surgical biopsy and ablative therapy.^{56,57} The choice of modality usually depends on the requirements for visualization and navigation needed for the procedure. Interventional MRI has several advantages including real time imaging of the needle and tumour with the absence of ionizing radiation. Interventional MRI needs to be dynamic, fast and able to properly show the MRI compatible interventional instrument with the relevant anatomy. Many of these challenges have been met. Soft tissue with poor contrast at US or CT is particularly useful for MRI-guided localization and treatment. Part of these requirements have been solved by the use of US-MRI fusion, mostly for prostate biopsy,⁵⁸ but there are inherent limitations regarding image acquisition during the treatments that can be overcome only by using MRI. Currently, real time fast pulse sequences are available on most MRI systems and computer power is adequate for immediate image and reconstruction. These sequences can be used to control the interventional tool using a simple freehand approach and an in-room monitor. The advantage of this approach is that very oblique interventional trajectories can be targeted in a sagittal plane. A skilled technician is required for manual adjustments and while the patient is inside the bore, manual manipulation is very limited.⁵⁹ Manipulators have been developed for needle navigation and provide a number of advantages over the free hand approach. Robotic manipulation achieves higher accuracy and shorter procedure time compared to the manual approach. Fine adjustments can be made with the patient remaining inside the bore and multiple biopsies can be made of the same lesion contributing to overall repeatability and safety. Both freehand and robotic approaches are used for treatment purposes.

Several forms of focal ablative treatments have been investigated the past few years. High-intensity focused ultrasound (HIFU), cryotherapy and focal laser ablation have positioned themselves as most promising for in bore use. MRI offers real-time quantitative thermometry maps and the visualization of critical anatomic structures such as nerves, bile ducts, bowel, bladder and ureter.⁶⁰ Combined with extended visualization of the ablation zone due to the possibility of multiplanar imaging and the excellent contrast between ice-ball formation/heat distribution and surrounding tissues provides unparalleled control of treatment.⁶¹ On the contrary, procedures were found to take longer under MRI control mainly because of patient preparation. In conclusion, interventional MRI is promising with regard to diagnostics, surgical biopsy and focal ablative treatments, enabling more possibilities and accuracy for interventional oncology.

Artificial intelligence in interventional oncology

In the current era, artificial intelligence (AI) is ubiquitously available. It is described as the technology in which 'computers mimic the problem-solving and decision-making capabilities of the human mind'.⁶² Although society tends to overestimate new technologies, it is likely that the use of AI in the field of medicine will increase in the years to come.⁶³ Multiple literature reviews have summarized which research has been done so far regarding AI in interventional oncology (IO), showing the expanding interest in this specific field.^{64–70} In general, research on AI in IO can be categorized in three functions: periprocedural assistance; patient selection, classification and outcome prediction; and finally patient follow-up.

For periprocedural assistance, several AI functions show potential for the use in the interventional suite. To begin with, deep learning for biopsy guidance, which is studied throughout the entire procedure from needle path planning to needle insertion, automatic needle segmentation and needle tip localization.^{71–74} This technology has led to a real-time tracking model of the catheter tip during catheterization procedures, which enables roadmapping of the vasculature without a contrast agent.⁷⁵ Touchless interaction is another AI function which has been examined, it enables the physician to give commands while under sterile conditions, such as activating lights, switching on and off components of medical devices, or even using hand and arm gestures to browse through sets of medical images without touch.^{76,77} Lastly, augmented reality (AR) and virtual reality (VR) could assist during IO procedures. While VR is mostly studied for teaching purposes, AR is experimented with in clinical practice for assistance during liver ablation and pulmonary biopsies.^{78–80} Specifically for pulmonary ground glass opacities, AR-assisted biopsies showed higher diagnostic accuracy for nodules <1.5 cm, a lower incidence in complications and a significant reduction of the administered radiation dose, compared to standard biopsies.⁷⁷

For patient classification and outcome prediction, studies frequently combine AI with radiomics. Radiomics is the field wherein medical images are converted into quantitative data that can be analysed using AI methods to determine the relationship between medical images and clinical outcomes.^{81,82} Radiomics is explored for various IO procedures. For example, multiple high-quality studies reached good performance in predicting outcome before transarterial chemoembolizations (TACE) in hepatocellular carcinoma (HCC).^{83–88} Transarterial radioembolization (TARE) has been investigated less extensively compared to TACE. Only some pilot studies have suggested radiomics features might be associated with outcome after TARE for HCC, liver metastases and intrahepatic cholangiocarcinoma.^{89–93}

Furthermore, good results were found for CT-radiomics predicting completeness of ablation in colorectal liver metastases, adrenal metastases and pulmonary malignancies.^{94,95} In addition, Ma *et al.*⁹⁶ used radiomics from contrast-enhanced ultrasound (CEUS) for prediction of recurrence in HCC lesions. Finally, the use of verification software for ablation evaluation and standardization of ablation margins needs to be implemented regularly in the clinical practice mostly in big lesions and/or with complex locations to optimize results.⁹⁷

More progress is required before the routine use of AI in clinical practices is possible and we need to overcome several challenges. Firstly, in comparison to diagnostic radiology, where there is universal data formatting (such as DICOM) and regulated imaging protocols, interventional radiology has more variance in imaging. For example, the type of intra-procedural imaging, the choices in imaging positions or timing and the use of specific devices are highly dependent on the treating physician preferences.⁶⁸ This variance makes it harder to collect a homogeneous patient cohort. Secondly, reaching the numbers needed to train AI applications might be problematic since some procedures are not performed often. This would require multicentre studies, which causes problems on its own due to centre and machine differences. Finally, the high rate of development and progress in IO could result in a need to update AI applications every time a treatment changes, raising questions of concern regarding feasibility. Despite the critical arguments mentioned above, promising results have come up in literature studying AI in IO, and its true potential needs to be fully explored. Radiologists working in IO should be open-minded to upcoming AI tools and applications to support and enhance their work, which enables them to strive towards a personalized tailored treatment for each patient.

Conclusions

There is a wide range of new technologies that offer several possibilities regarding image guidance for interventional oncology. The nature of the centre and the physician preferences are capital to choose the best guidance, always keeping in mind the importance of reducing the radiation doses and maximizing the results. The advent of different AI techniques will allow for an optimization in the selection of these modalities and their use in each clinical scenario. It will also permit physicians from other specialties different from radiology to be involved in IR procedures making a challenge not losing our current position in that field.

Data availability statement

Data sharing not applicable – no new data generated.

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