

Technological Advancements in Interventional Oncology

Subjects: **Oncology**

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Interventional radiology, and particularly interventional oncology, represents one of the medical subspecialties in which technological advancements and innovations play an utterly fundamental role. Artificial intelligence, consisting of big data analysis and feature extrapolation through computational algorithms for disease diagnosis and treatment response evaluation, is nowadays playing an increasingly important role in various healthcare fields and applications, from diagnosis to treatment response prediction. One of the fields which greatly benefits from artificial intelligence is interventional oncology. In addition, digital health, consisting of practical technological applications, can assist healthcare practitioners in their daily activities.

interventional radiology

interventional oncology

artificial intelligence

digital health

1. Radiomics

Radiomics is a science which combines radiology, mathematics and artificial intelligence techniques, using data-characterisation algorithms and mathematical analysis to extract many aspects and traits from radiological imaging; it performs a quantitative approach to diagnostic imaging acquisitions, as opposed to the classical qualitative approach made by physicians [1]. Radiomics evaluates the so-called image biomarkers as digital image texture, consisting of the single pixels and their relationship to the other pixels, as well as intensity and tissue density spatial distribution; these traits, known as radiomic features, may reveal tumoral patterns and characteristics that are not visible to the human eye. The various phases to obtain radiomics features consist of data collection, target lesion segmentation, image biomarkers detection and extraction from image texture, modeling, processing, and validation [2]. The unique imaging characteristics of different disease forms may be helpful in predicting the prognosis and therapeutic response of different types of cancer, thereby offering important information for individualized treatment. The most cutting-edge uses of radiomics are found in radiology and oncology, and therefore, in IO.

1.1. Diagnosis

DL systems based on convolutional neural networks (CNNs) have shown potential to revolutionize the process of radiological diagnosis, increasing sensitivity in classifying neoplastic lesions, and giving the radiologist the ability to interpret, check and validate the results [3][4][5]. AI plays an important role in IO, helping physicians to achieve a

higher accuracy in the diagnosis of lesions and, thus, to choose the best approach to treatment, personalized for every patient and every neoplastic lesion.

In their study, Hamm et al. tried to develop and validate a DL system based on CNNs, which classifies common hepatic lesions on multi-phasic magnetic resonance imaging (MRI), and compared its performances with those of diagnostic radiologists; test set performance in a single run of random unseen cases showed an average 90% sensitivity and 98% specificity, while the average sensitivity and specificity on these same cases for radiologists was 82.5% and 96.5%, respectively. Results showed a 90% sensitivity for classifying hepatocellular carcinoma (HCC) compared to 60–70% for radiologists [3]. Moreover, the authors have attempted to develop a proof-of-concept “interpretable” DL prototype that justifies the aspects of its predictions from the pre-trained hepatic lesion classifier, identifying and scoring radiological features. This method enables radiologists to interpret elements of decision-making behind classification decisions; this way, clinicians can validate these features by using feature maps or similar interpretability techniques and can check whether the system has accurately identified the lesion’s features in the correct locations [4]. Yasaka et al. in their clinical retrospective study investigated whether different types of liver masses could be differentiated at dynamic contrast agent-enhanced CT by using models based on DL with a CNN. Masses were diagnosed according to five categories (category A, classic HCC; category B, malignant liver tumors other than classic and early HCCs; category C, indeterminate masses or mass-like lesions—including early HCCs and dysplastic nodules—and rare benign liver masses other than hemangiomas and cysts; category D, hemangiomas; and category E, cysts). DL with CNN showed high diagnostic performance; median accuracy of differential diagnosis of liver masses for test data was 0.84 and median area under the receiver operating characteristic (ROC) curve for differentiating categories A-B from C-E was 0.92 [5]. The great promise of AI in interventional oncology is to bring precision medicine at its finest, to the level of the individual patient, through a better understanding and definition of the target lesion. Budai et al. retrospectively constructed a radiomics-based model to diagnose histotypes of renal cell carcinoma (clear-cell versus other histotypes) evaluating the CT scans of 209 patients with renal cell carcinoma, obtaining an accuracy of 78%, sensitivity of 80%, and specificity of 74%, respectively; these results were compared to the ones achieved by an expert radiologist (accuracy of 79%, sensitivity of 84%, and specificity of 69%) [6].

1.2. Staging and Outcome Prediction

Staging and outcome prediction is mandatory to address the best treatment for every patient, and this also applies to IO in which locoregional treatments greatly vary based on tumor staging and patient’s outcome, particularly for HCC patients [7].

Most of the current staging systems (e.g., the Tumor, Node, Metastasis (TNM) classification) have limitations in terms of patient prognosis. On the other side, nomograms represent a useful tool in personalized care of oncologic patients, used by an increasing number of cancer centers to improve clinical practice. Nomograms are getting more and more useful in oncological settings as they are capable of estimating the personalized patient risks and prognosis based on disease and subjective characteristics. Even though nomograms’ diffusion dates back to before AI’s, artificial intelligence plays a great role, integrating prognostic and determinant variables, generating a

personalized and individualized probability of a patient's clinical event. Nomograms can be obtained for virtually all types of cancer and can predict various outcomes (prognosis at the time of diagnosis, post-treatment recurrence risk, procedure-specific survival outcomes).

AI-based nomograms with easy-to-use digital interfaces allow for fast and accurate data computation, obtaining clearer and easier to understand prognoses compared to other staging systems, improving the decision-making process. Gupta et al. retrospectively investigated CT images texture to predict grading and survival of 38 patients with suspected gallbladder neoplasm [8]. Multiple authors used radiomics-based models to predict lymph node metastases in various cancer types (e.g., gastric, breast, bladder, colo-rectal) [9][10][11][12]. AI-based tools can also be used for the staging of the primitive tumor, as well as for prediction of aggressive disease progression [13][14][15][16]. These studies demonstrate how AI outperforms "classical" staging systems, and better determines tumor stage and presence of metastasis, granting a more accurate, personalized and faster treatment choice.

1.3. Treatment Response Prediction

ML and DL models can be used in IO practice in predicting response to treatment of cancer patients undergoing locoregional (percutaneous or intra-arterial) therapies. Artificial neural networks that are multilayered or "deep" are the basis of DL. The various neural layers between input and output provide the DL with its plasticity and the ability to define novel patterns of intelligent classification, simulating the workings of the human brain. When compared to a human reader, who can only detect and use a portion of the total big information content of digital images, DL can automatically distinguish the pertinent features from data, allowing it to learn new patterns and determine more complex relationships. This is particularly true in IO where DL-models are capable of integrating multiple patient and tumoral variables, unseen at the human eye, to guide clinical choices and to predict outcomes of locoregional treatments as transarterial chemoembolization (TACE), radioembolization (TARE), and percutaneous ablation.

2. AI-Assisted Detection and Segmentation

Computed-aided detection (CAD) is an increasingly utilized tool to perform an adjunctive, second read of diagnostic imaging acquisitions (X-ray, CT, MRI) in order to assist the radiologist in the detection of pathologic lesions and improve their accuracy. Mostly used on chest X-rays and lung CT scans for pulmonary nodules [17][18]. Lee et al. evaluated the efficacy and clinical usefulness of lung nodules' CAD in patients with colorectal cancer oligometastases to the lung, obtaining good sensitivity and specificity values [17]. Li et al. demonstrated how the recent technological advancements of CAD recognition algorithms increased the accuracy of lung nodule detection up to 99.56%, with a sensitivity of 99.3%, greatly reducing false negatives and missed detections [18]. Ahn et al. determined the usefulness of evaluating breast MRI with a CAD software in the prediction of invasive neoplasm in patients with ductal carcinoma "in situ", to select patients for sentinel lymph-node biopsy [19]. Takamoto et al. validated a recently developed software of AI-assisted CT-based virtual hepatectomy in patients affected by liver cancer, with a focus on processing time, obtaining reliable and accurate volumetries with a significantly ($p < 0.001$) shorter processing time for AI-assisted reconstructions [20]. AI-assisted CNN-based virtual segmentation can

also be useful and time-sparing for volumetries prior to transarterial radioembolization procedures, as demonstrated by Chaichana et al. [21]. The authors developed an automated CNN-based method for target lesion and organ segmentation on Single-Photon Emission Computed Tomography (SPECT) images obtained after ^{99m}Tc -labeled Macroaggregated Albumin (MAA) administration, obtaining a time-sparing (about 1 min per patient) and accurate segmentation method. CAD can be an extremely valuable tool for interventional radiologists, as it can provide a faster and more efficient way to detect small or barely visible lesions, leading not only to a correct and early diagnosis but also to a shorter time-to-treatment for patients, which can eventually lead to a better prognosis. As previously stated, CAD may also help IO practitioners to reduce the planning time, as in the case of pre-procedural hepatic volumetric assessment.

3. Digital Health

3.1. Virtual Reality and Augmented Reality

Digital reality, or extended reality, is an umbrella term which covers all the various technologies that enhance human senses, including platforms that represent cutting-edge technology and that will transform medical training and clinical practice at its most routine levels and at its highest technological point, to drive adoption quality and confidence in performing new procedures with new devices [22]. Nowadays, various forms of digital reality are available and continuously improved:

- Augmented Reality (AR) consists of the addition of digital elements to a live view, basically creating a hybrid of our own reality view and computer-generated objects;
- Virtual Reality (VR) is a completely digital view, where objects and the environment are being replaced by fully digital elements;
- Mixed Reality combines elements of both AR and VR, bringing a technology in which real-world and digital objects simultaneously interact with each other.

One of the most promising digital reality applications is probably navigation, which makes possible many tasks such as layering of medical 2D or 3D images, establishment of the skin entry point, display of the target lesion, visualization of the needle path, identification of structures that should be preserved or are vulnerable in the needle path and also tracking of the distance and angle to target lesions. A traditional CT setup has a monitor directly in front of the scanner, allowing the physician to analyze images and process data on the scanner table with the assistance of a position laser or a laser guide and the sporadic use of in-and-out CT imaging acquisitions to determine the instrument's position. However, this traditional CT setup lacks real-time feedback information on images, needle position and anatomy, which is where AR may be helpful. MRI can be a challenging modality for interventional procedures since it has longer acquisition time and gantry- as well as magnetic-field-related issues; however, these interventions can be particularly facilitated by AR navigation. A prototypical setup for a navigation system, described in the literature by Fritz et al., uses AR to perform navigation, identification of the anatomic site

and of the needle path from the outside, and includes an MRI scanner (or a CT or any hybrid scanner), a dedicated workstation, and a navigation unit. The navigation unit can consist of an MRI-compatible monitor and a semi-transparent mirror to reflect the monitor. Imaging data are acquired and, subsequently, an overlay system allows projection into the mirror and from the mirror into the line of the interventional site; the operator sees both the patient and the MRI (or CT) images or other superimposed information through the semi-transparent mirror. Regardless of where the operator stands, the images are always following, with a laser projected into the skin for determination of the entry point. The display can be mounted with a frame, can be attached to the scanner, or can be freely standing on the other side of the scanner [\[23\]](#).

Some limitations of AR were described in the recent past, but most of them are nowadays partially or completely resolved, such as:

- The limited field of view (human eyes have a field of view of 200 degrees in horizontal plane and 135 in vertical plane, while head-mounted displays (HMDs) have a field of view of less than 90 degrees);
- Hardware efficacy (however, nowadays even cheaper smartphones meet the minimum requisites);
- Registration mismatch between the real target and the visualized target, or between target and interventional device (which nowadays is less than 5 mm);
- Cybersickness (nausea, headache, dizziness, and vestibular mismatch that can be brought up while using HMDs; however, these symptoms are nowadays dramatically reduced even though subjective to the single physician);
- Time-consuming user-dependent calibration and adjustment with HMDs (no longer needed or greatly decreased nowadays);
- Weight of HMDs.

The main advantages of guidance with AR consist in the significant reduction of radiation dose for procedures performed in the CT room (thanks to the pre-procedural integration of data and minor use of radiographic guidance), system usability both in ultrasound and CT room, for every organ and with any device, high speed and great precision. AR has the potential to change the interaction between imaging formation and clinical practice.

3.2. Robotics-Assisted Ablation

Robotics in IO can be of great help as could make treatments available also in countries which lack adequate access to IR specialists. Routinary use of robotics in IO can lead to the reduction of radiation exposure to operators and can increase procedure accuracy in the near future. Robotics systems offering off-plane and multiplanar percutaneous intervention planning, targeting, as well as needle positioning, also using three-dimensional target views, are available for clinical use and can easily support practitioners [\[24\]](#). Image-guided systems can be useful

for spatial positioning and orientation of one or more ablative needle-probes, assisting in manual advancement of the probe (electrode, antenna, etc.) and as intraoperative guidance and post-treatment verification [25]. Robotics-based systems with remote micro- and macro-positioning of the needles can be used for interventions with CBCT, fluoroscopy, and CT in which needle placement is operated by the physician but from a distance [26]. A recent study showed that a table-mounted CT-robot succeeded in reducing microwave ablation needle repositioning attempts and increased accuracy for out-of-plane targets (5.9 mm versus 10.1 mm) but at the cost of longer targeting time compared to freehand targeting (36 min versus 19 min) [27]. CT-guided steerable mini-robots probably represent the most advanced and useful technology in IO nowadays: this robotics-based system is capable of intraprocedural correction of trajectory misalignments during percutaneous procedures [28]. However, many unsolved issues are still under investigation such as cost-effectiveness, standardization, high learning curves, impact on workflow, and so on.

3.3. Virtual Multidisciplinary Tumor Board

Integrated multi-disciplinary assessment of every oncological patient undoubtedly leads to better clinical decisions. Virtual multidisciplinary tumor board (v-MDTB) platforms can offer the power to visualize, support, diagnose, and communicate, integrating data from hospital information systems across different clinical domains (such as radiology, pathology, and genomics), thus enabling a consistent, comprehensive, and intuitive view of patient's relevant information and care path, to facilitate cross-disciplinary collaboration and communication and giving the physicians evidence-based decision tools to promote guidelines adherence and evidence-driven care in personalized medicine. Interactive conferencing, in which a three-dimensional tool can be created, allowing us to virtually discuss how to approach certain percutaneous interventions, can be done with all the physicians together in one room or through teleconferencing [29].

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