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Imaging science and development in modern high-precision radiotherapy

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The use of imaging data in radiation oncology has a long tradition. Since the first idea of 'dose painting' [1], anatomical and functional imaging modalities have been reported to improve and personalize radiotherapy (RT) (Fig. 1) [2-4]. Computed Tomography (CT) has been used for more than three decades for three dimensional (3D) target volume and organ at risk delineation as well as for accurate dose calculation, due to the inherent representation of mass or electron density values of the underlying tissue. Moreover, cone-beam CT imaging has found its way into clinical usage for position verification before and during delivery of fractionated RT [5,6]. More recently, magnetic resonance imaging (MRI) has been proposed for online image-guided RT in hybrid MRI linear accelerators (MR-Linacs) [7–11]. Functional MRI and positron emission tomography (PET) have been shown to be able to guide personalized RT applications in terms of dose painting where the first studies are currently on their way [12-16]. Similarly, different imaging biomarkers are currently being investigated for their potential to predict tumor outcome and side effects after RT [15-17]. To realize these various applications of imaging in RT, dedicated methods and tools for image acquisition, reconstruction, post-processing, registration and analysis are required. These methods include research areas such as radiomics, artefact reduction strategies or analysis methods for timeresolved imaging data, with a special focus on the needs of RT applications [18-20].

Almost three years ago, the first issue of *physics and imaging in Radiation Oncology (phiRO)* was launched. The journal aims at publishing studies reporting investigations in the field of medical physics and imaging sciences devoted to improving RT planning and delivery. Since early 2017, more than 50 articles were published in phiRO reporting on different aspects of imaging for radiation oncology, corresponding to around half of the published papers. These imaging papers focus on different aspects of imaging in radiation oncology and show thus nicely the spectrum of imaging applications for RT planning, delivery and outcome prediction.

1. CT imaging for RT

Since the invention of CT imaging as a method to visualize 3D maps of mass or electron density, CT-based RT planning is standard of care for the vast majority of RT patients. Nevertheless, research in the field of CT imaging is still ongoing to improve image quality and reduce artefacts for more accurate dose calculation by using e.g. novel reconstruction algorithms [21–25]. With the clinical availability of proton therapy, the requirements for CT-based density estimation changed enormously as stopping power determination and dose calculation depend strongly on the tissue composition [26,27]. Consequently, dual energy CT (DECT) was proposed as an alternative CTtechnique for proton therapy planning [28–34]. Furthermore, timeresolved CT imaging, so-called 4D-CT, has been shown to inform about tumor and organ motion and thus provide valuable information to be integrated into RT planning and delivery [24,35,36].

2. CBCT for RT position verification and adaptation

Onboard CBCT imaging has proven its clinical value for inter-fraction patient positioning for high-precision RT. Furthermore, new strategies to base RT dose calculations on CBCT data are currently explored [37,38]. In recent research projects, new methods were investigated to improve 4D-CBCT functionality in order to assess intra-fraction motion of moving targets and to suggest strategies for treatment adaptation [39–41]. Furthermore, accurate simulation of radiation dose contributions resulting from repeated CBCT examinations have been investigated in detail by several groups [42–45].

3. MRI-guided RT

Due to its high geometrical resolution in addition to an excellent soft tissue contrast, MRI is a powerful imaging technique for imageguided RT. Thus it has potential for improving target volume delineation, offline and online plan adaptation and therefore provides the basis for personalization of RT [46,47]. In the last years, a variety of research projects investigated the value of using additional MRI data for target definition. Consequently, an important technical focus was the characterization and improvement of MR image quality and artefact reduction [48-52]. MRI offers higher soft tissue contrast for tumor and organ definition but lacks information about electron density, which is a prerequisite for accurate dose calculation. To overcome this, several groups have proposed strategies to generate synthetic CT data sets derived solely from MRI data [53-56]. First dosimetric analysis of such MR-only workflow showed quite promising results for tumors in the pelvic region [57]. Recently, hybrid MR-Linacs are clinically available and offer online MR-guided RT. Physical challenges of MR-guided adaptive RT concern treatment planning and dose calculation in magnetic fields [58-63] and strategies for MR-based RT plan adaptation with minimal latency time [64,65]. In the future, imaging biomarkers assessed from functional MRI may be useful for the prediction of therapy outcome or side effects after RT [66-68].

4. Functional imaging using PET and MRI for personalization of RT

Several recent studies have investigated the role of multimodal functional imaging to stratify patient groups and individualize RT dose prescriptions and treatment planning / application strategies according to imaging information [69–72]. PET data has been shown to have

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Fig. 1. Different imaging modalities and strategies for using anatomical and functional imaging data in radiation oncology.

great prognostic potential in different tumor entities [73,74] opening new possibilities for target volume definition [75]. Furthermore, the value of functional MRI, such as diffusion weighted imaging (DWI) [76–78] and perfusion imaging using dynamic contrast enhanced (DCE) MRI [79,80] for outcome prognosis of functional image guided RT planning has been investigated. Further studies have analyzed the combined information from multi-modal PET and MRI [75,81] for biologically adapted, personalized RT [82].

5. Image data processing, analysis and radiomics

With increasing availability of large amounts of imaging data, robust and reproducible ways for image analysis, integration and exploration are needed. Recent studies have investigated the potential of radiomics for precision RT [19,83–85]. Of note, for high quality usage of functional and anatomic imaging data, dedicated robust strategies for image registration [86–89] and data analysis [90] are needed. Only then, reliable new segmentation algorithms [91,92] and prediction models can be trained [16,93].

In conclusion, imaging in radiation oncology has many facets ranging from dose calculation to outcome modeling. With increasing availability of anatomical and functional imaging modalities, the benefit and potential of using these technologies and the respective imaging data dedicatedly in radiation oncology to further improve the effectiveness of cancer treatment with RT are eminent. Nevertheless, integration of imaging data into planning and application of precision RT will be a key factor for future developments in personalized RT. Acknowledging the important role of imaging in radiation oncology, phiRO is now broadening its editorial composition with the appointment of a 2nd co-Editor-in-Chief dedicated to imaging (Daniela Thorwarth). With this in place, phiRO is fully prepared to receive your submissions from all areas in this expanding and vital area of radiation oncology, and to make sure that your research findings are structured and presented for publication in the best possible way.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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