Editors Picks

MRI-based tumour control probability in skull-base chordomas treated with carbon-ion therapy

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What was your motivation for initiating this study?

The main idea of our study was to investigate the contribution of MRI to treatment outcome prediction in carbon-ion radiotherapy (CIRT). We derived information from MRI data to personalise models of tumour control probability (TCP) in a cohort of skull-based chordomas treated with CIRT at the National Centre of Oncological Hadrontherapy (CNAO, Pavia, Italy).

Standard TCP models link the planned dose to a certain outcome measure, relying on population-based radiosensitivity parameters1. This raises the question of whether and how patient-specific information can be included in such models. Although radiosensitivity parameters (i.e. α and β from the linear-quadratic cell-kill model) play a major role in TCP modelling, their in-vivo estimation has not yet been achieved. Instead, routinely acquired functional imaging could provide personalised information about, for example, oxygenation and cellularity, which are known to impact treatment outcomes to variable extents. Our initial hypothesis was that functional imaging could help to improve TCP models in CIRT for which, due to its high radiobiological effectiveness, a bespoke description of treatment-related effects is required.

Inspired by previous work on prostate patients2 and relying on published experimental data3, we retrospectively gathered pre-treatment diffusion-weighted MRI (DW-MRI) to compute cellular densities in skull-base chordoma tumours from apparent diffusion coefficients (ADC) to personalise an MRI-based TCP model.

What were the main challenges during the work?

The main challenge we encountered was the lack of experimental data for skull-base chordomas, both in terms of radiosensitivity and of correlation between ADC and tumour microstructure.

Regarding the lack of experimental information, data from in-vitro experiments1 greatly helped us to understand and evaluate the feasibility of our approach. However, the data in the published literature did not match our patient cohort, so we were forced to devise an ad-hoc methodology to estimate α and β parameters.

Regarding the second aspect, we linked DW-MRI to cellularity by exploiting a correlation study performed on a heterogeneous cohort patient group that included, among others, a few cases of skull-base chordomas. Such relationship needs to be strengthened by a validated and precise link between DW-MRI and microstructural parameters, possibly tailored to chordoma patients. To tackle this challenge, both population-based studies and advanced MRI sequences could help to better match between microstructural and diffusion data. This approach would better suit treatment personalisation.

Additionally, the accurate combination of dose maps, computed through the geometrically precise CT imaging, and functional DW-MRI imaging, known to be affected by geometrical distortions, remains an open issue. Deformable image registration4 for dose warping and spatial normalisation studies5 need to be investigated and put forward to propose reliable and automated clinical workflows.

What is the most important finding of your study?

With this study we provided evidence of how MRI-derived information can be included in clinical workflows in particle therapy. We showed that patient-specific information increases patients' differentiation with respect to population-based approaches and predicts more conservative tumour control probabilities.

What are the implications of this research?

The main implication of this study is that functional imaging can nourish personalised particle therapy, with future consequences for treatment definition and the development of image-guided particle therapy.

Radiotherapy treatments, especially advanced ones such as CIRT, would benefit from patient-specific applications in terms of outcome. We expect that the definition of personalised prediction models will lead to tailored adaptive treatments and dose escalation strategies, as confirmed by current trends in the field6.

At the same time, a detailed multi-scale relationship between clinical imaging and tissue functionality, which affects its radiosensitivity, could effectively link patient and experimental data. MRI is an optimal candidate on which to base such a link because of its flexibility and capability in describing tumour response to therapy. We believe that radiation oncology should look into advanced MRI sequences7,8 that provide accurate functional information, in terms of tissue organisation, cellular density and membrane integrity. If and when this transition happens, data-based studies3,9 will retain their potential in predicting tumour response to treatment for most of the common tumours, though they will be limited in case of rare cancers, which will require deeper investigations considering that small datasets are available.

In our opinion, this approach lies between the use of analytical models defined at the micro-scale and data-based models defined at the patient level, as it works across scales (DWI vs. cellularity) to tailor treatment predictions. Moreover, it is one of the first attempts to integrate quantitative MRI into particle therapy, and we put it forward as groundwork for further developments in personalised CIRT.

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