Teaching Lecture: The integration of multimodal imaging in the radiation treatment process: pitfalls and challenges

SP-0005
The integration of multimodal imaging in the radiation treatment process: pitfalls and challenges
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Radiation oncology is a rapidly evolving specialty. In analogy with the evolution from conventional radiotherapy over 3D conformal radiotherapy to intensity modulated radiotherapy and volumetric modulated arc therapy, there has been a shift from the use of anatomical imaging (e.g. CT, MR) to functional imaging (e.g. DW-MRI, DCE-MRI) and biological imaging (e.g. 18F-FDG PET). In the current process of radiation treatment, the radiobiological response of tumor and normal tissue in patients is monitored non-invasively by a variety of imaging techniques. Integration of these imaging techniques into therapy selection strategies and radiation treatment can serve several purposes. First, pre-treatment assessments can steer decisions on the radiation treatment as such or on the combination with other modalities. Second, biology-based objective functions can be introduced into the radiation treatment planning process by co-registration of molecular imaging. Relevant radiobiological parameters that can be assessed include tumor burden, tumor hypoxia, tumor proliferation and tumor metabolism. This would allow us to generate customized heterogeneous dose distributions with escalated doses to tumor areas where radiotherapy resistance mechanisms are most prevalent. However, there are some hurdles to overcome including the discrepancy between resolution of imaging techniques and spatial scale at which radiosensitivity is determined and the treatment induced temporal and spatial changes in tumor morphology and biology.

Third, monitoring of temporal and spatial variations in these radiotherapy resistance mechanisms early during the course of treatment can discriminate responders from non-responders. With such information available shortly after the start of treatment, modifications can be implemented or the radiation treatment plan can be adapted based on the biological response pattern. In this teaching lecture, some background on the different imaging techniques at our disposal for early response monitoring will be given and examples of current applications and future perspectives for the further integration of imaging in the radiation treatment process will be shown.

Teaching Lecture: How to manage geometric uncertainties

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How to manage geometric uncertainties
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Uncertainties are still a major challenge in cancer treatment. The resulting deviations between planned dose and delivered dose need to be minimized. The widely used PTV-approach contains several pitfalls. Firstly, it is based on a single patient-snapshot in time, whereas patient treatment is a dynamic process. Secondly, expanding the clinical target volume (CTV) to the planning target volume (PTV) always entails an increased dose in the organs at risk (OARs). Lastly, it is geared towards geometric uncertainties in conjunction with conventional radiotherapy and fails in hadron-based therapy. For more than a decade, alternate approaches have been an active area of research. Thus, there is a multitude of methods to be found in literature. While their sheer number can be overwhelming, the vast majority fits in two distinct categories. On one hand, there are methods that strive to control the dose to each element in a volume of interest. On the other hand are algorithms, that control the outcome metric (e.g. max dose, equivalent uniform dose (EUD)). Even though they have considerably different prerequisites, strength and weaknesses, they share the common goal of target dose escalation and/or improved OAR sparing. This also and especially includes non-conventional modalities such as hadron-based therapy. Fortunately, with the increasing availability of imaging information, the wide-range deployment of next generation treatment planning via such methods is feasible. This teaching lecture will elaborate the general differences between both schools of thought, as well as present their similarities. It turns out that, upon closer inspection, even a quantitative relation can be established. The lecture will also include an excursion into algorithm-internal uncertainty management. More specifically, it will cover effects that arise from finite sample sizes, e.g. due to a limited number of images available at the time of planning. The impact of treatment fractionation on uncertainty handling will also be touched upon. It is the ultimate goal of the lecture to build a mind map about different kinds of uncertainties, and how they may be tackled. This will be underpinned with an exemplaric overview of current literature.

Teaching Lecture: Use of imaging to predict toxicity and tumour control

SP-0007
Use of imaging to predict toxicity and tumour control
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Medical images of various modalities are important factors in establishing diagnosis and stage of the disease, and are used extensively before, during and after radiotherapy of cancer patients. However, from treatment planning is commenced until radiotherapy has ended, image information is except for the dose calculation usually considered only in a very strict geometrical sense: To define the target and delineate critical structures on planning images, and to realign the patient in a geometrical sense: To define the target and delineate critical structures on planning images, and to realign the patient in a
Response evaluation after radiotherapy can be used to make population based recommendations, but is untimely to influence the delivery of radiotherapy on an individual patient basis. There is an active search for associations between medical image features obtainable before or early during the treatment course and radiological finding, clinical symptoms, and tumor control after radiotherapy. Such a predictive assay can be related to either normal tissue or tumor response on a per patient basis. Ideally the assays should include both normal tissue and tumor response since intensified treatments typically are related to an increased probability of intolerable toxicity. A source of medical image information during radiotherapy is Cone Beam CT (CBCT). Patient specific density changes of normal lung tissue are observable in CBCT images and publications on dose response relations during the first part of the treatment are available. These observations might show a way to a predictive assay of toxicity based on CBCT images. Also tumor volume changes are observable during RT in CBCT images, and have in a few publications been shown to be associated with local control as well as overall survival. Pretreatment PET images are another candidate for a predictive image assay. Several research groups have published associations between PET signals before treatment and overall survival. If these results can be confirmed in independent studies, PET imaging might be used to select patients for escalated radiotherapy. A key issue in evaluation of medical images is the image quality which has been ever improving. One of the more recent improvements has been development of 4D imaging which reduced blurring artefacts. 4D images have made it possible to evaluate ventilation of specific regions of the lung and it has been suggested that avoidance of irradiation of highly ventilated areas of the lung could impact the expected toxicity level. Also changes in ventilation during radiotherapy might potentially carry information of likely level of toxicity. Predictive assays based on medical images remains a developing field with a potential to generate “free of charge” information, since the medical images are already available due to their current geometric use. Examples, primarily related to lung cancer, of different attempts to establish relation between image features and toxicity or tumor control will be presented and their potential impact addressed. Furthermore, attempts to further improve image quality will be commented upon since the image quality might be the limiting factor in establishing reliable predictive assays based on medical images.

Teaching Lecture: Theory of margin calculation: How far can we reduce our margins?

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Theory of margin calculation: How far can we reduce our margins?
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Introduction: With the advent of image guided and adaptive strategies the management of position variability has become commonplace. Nevertheless, margins are still required to account for the remaining uncertainties. However, since the origin and/or magnitude of these uncertainties is not always clear, there is a risk of applying too small margins. The purpose of this presentation is to describe the process of determining a margin, and to identify all factors involved. Margins: The current theory of margin calculation is based on group statistics, i.e., the margin is designed in such a way that a certain percentage of patients (e.g. 90%) is adequately covered. This approach is necessary, as not all patient specific errors are known at the time of treatment planning. For the actual computation of the margin it is important to distinguish systematic and random errors separately, as their effect on the margin is quite different. Random errors, generally denoted by a standard deviation σ, are different every day and cause a blurring of the dose distribution that requires a relatively small margin. Systematic errors, denoted by a standard deviation Σ, shift the dose distribution and require a considerably larger margin. In its most simplistic form, assuming a spherical CTV and a large number of fractions, the margin to cover 90% of all systematic errors with 95% of the prescription dose is approximately 2.5Σ + 0.7σ.

Geometrical uncertainties: The major contributing factors to the total geometrical uncertainty are delineation, setup and organ motion. While the latter two will cause both systematic and random errors, delineation uncertainty is a purely systematic error source. For setup variation and organ motion, both inter- and intra-fractional errors are distinguished, with the latter usually being considerably smaller than the former. Other errors that can be significant are registration inaccuracy, planning system related factors (e.g. beam fits) and machine related delivery errors. For example, registration inaccuracies will impact the delineation uncertainty when using multiple modalities, and the accuracy of image guidance.

Image guidance and residual errors: Most image guidance strategies today aim to minimize the random and/or systematic geometrical uncertainties by offline or online correction protocols based on either surrogates or the actual tumor position, and are usually limited to translational corrections. Therefore, rotational errors, shape changes, and intra-fractional changes are not corrected for. Furthermore, once the major contributors to the uncertainty (setup, organ motion, delineation) are dealt with, other errors, e.g. registration and treatment delivery errors, may become significant. Not taking these uncertainties into account when designing the margin will result in geometrical misses and possible reduced tumor control. On the other hand, the commonly used margin formula relies on a number of assumptions which may lead to an overestimation of the required margin. For example, one of the assumptions is that under-dosage to any extent is not tolerated at all, which may well be true for a GTV but may be ok to some extent for a CTV where there is only a probability of disease. Therefore, more complex methods of evaluating adequate dose distributions, e.g. probabilistic planning may be required.

Discussion and conclusions: There are many factors that determine the required margin. Delineation uncertainty, setup errors, organ and tumor motion are important, but once these errors are managed, other smaller errors will become significant and ultimately limit how far we can reduce our margins.