Image Guided RadioTherapy (IGRT) is currently considered the golden standard in radiotherapy. Especially IGRT is required for prostate cancer, as the prostate is a small organ, which can show large movements and where the actual tumor inside the prostate is difficult to detect. Imaging in prostate cancer IGRT can be divided into (1) imaging before treatment for patient selection and treatment planning, (2) imaging during treatment to compensate for movement and (3) imaging after treatment to evaluate treatment success or to detect a local recurrence.

1. Imaging before treatment consists of a CT-scan and an MRI scan for delineation and planning purposes. MRI has optimal soft-tissue contrast and adds to the CT delineation, especially as it is able to show the location of the tumor inside the prostate. MRI usually consists of both anatomical sequences (T1-, T2-weighted) and functional imaging, like perfusion (DCE-MRI), water diffusion (DWI), metabolites (MRS), and several other possibilities (Figure 1). As the information on the location of the tumor in most sequences does not overlap, decisions are required to delineate the tumor. Predictive models are currently developed to help this decision. For detection and possible treatment of regional metastases and/or bone metastases MRI and Choline-PET are currently investigated.

2. Imaging during treatment is meant to compensate for movement. Visualization of gold fiducial markers can be used for this purpose, but also Cone-beam CT is commonly used. An MRI-linac is under development. In brachytherapy, ultrasound is generally used for intra-fraction decisions. Currently, brachytherapy (HDR and LDR applications) is being developed in the MRI.

3. Post-radiotherapy a Choline PET is used to detect local recurrences. Imaging in prostate cancer IGRT can be divided into (1) imaging before treatment for patient selection and treatment planning, (2) imaging during treatment to compensate for movement and (3) imaging after treatment to evaluate treatment success or to detect a local recurrence.

Image registration - the fusion of volume image data sets acquired with different modalities or at different points in time – has become a vital tool for radiotherapy planning in cases where hybrid imaging techniques are not available or not feasible. Applications range from comparison of target volumes over time to multimodal image fusion, compensation of inter- and intrafractional target volume motion, adaptation of dose plans and precise patient setup in image-guided radiotherapy. The topic of this lecture is to introduce the basic methods of image registration and to highlight the possibilities and limitations with a special view on the requirements of radiotherapy. An overview of clinical applications and research perspectives will be given.
Tissue characterisation for radiotherapy

The purpose of this teaching lecture is to examine typical approaches for representation of patient anatomical data in treatment planning systems and the impact of that representation on the accuracy of dose calculation.

Dose calculation in modern treatment planning systems, which can often report dose to water or dose to medium, require mass density and tissue composition information for accurate accurate kernel scaling and radiation transport. The planning systems use patient specific anatomical information in the form of high-resolution CT images for volume definition and dose calculation. CT information is obtained at kV energies so in order to obtain the relevant properties required for use in high-energy photon or proton beams the CT numbers are converted to electron density or proton stopping powers using calibration curves obtained using phantoms with known properties. Following this, the patient data is resampled into a more coarse matrix and then segmented into a limited number of tissue types based on, for example, data from ICRU44 or ICRP23, which are themselves obtained from population based data sets. Dose calculations are performed on these converted, re-sampled data sets and output as distributions on the original high resolution CT image set. Errors at the conversion stage can propagate through to dose calculation and the number of tissue sets used in the conversion process has been shown to have an effect on the dose calculation. In particular, for low energy ranges including brachytherapy energies, it has been shown the assignment of tissue properties can significantly affect dose calculation, e.g. by recalculating the actually given dose using the CBCT image, would be a necessity. But maybe the most challenging part is finding the time and resources to be able to truly utilize all benefits that volumetric imaging is offering us.

Improving treatment accuracy: new challenges in positioning, immobilisation and verification

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In-room patient imaging started in the 1950s. Different initiatives were taken to monitor and improve patient’s treatment positioning. Not earlier then the 1990s Electronic Portal Imaging (EPI) was developed and became commercially available. The development of EPI much improved both the process and the quality of the verification of the treatment position. The role of EPI grew and became an important part in the quality assurance (QA) chain of radiotherapy.

In the last decade, 3D volumetric imaging was introduced. Nowadays most vendors have some kind of 3D imaging device commercially available. One advantage of 3D imaging is the improved quality of patient registration. Different studies showed improved registration accuracy as compared to 2D EPI. Another advantage is the ability to register patients directly to the tumour, e.g. in case of lung cancer. This not only contributes to the widespread application of Stereotactic Body RadioTherapy (SBRT), but it also resulted in more insight in fundamental processes like the baseline shift of lung tumours. Knowledge about these processes further underlined the importance of 3D image guidance.

More recent, the application of Adaptive Radiotherapy (ART) has increased and in-room volumetric imaging is a basic requirement for many types of the sophisticated treatment. For instance, in the Plan-of-the-day concept a treatment plan is selected daily from a library of plans based on the actual size/shape of the tumour as visualised with Conebeam-CT (CBCT) images. This type of treatment has been introduced for treatment sites like cervix and bladder cancer. Developments like ART force us to look at the changing physiology and pathology of patients. There is a growing evidence, however, for monitoring anatomical changes over the course of radiotherapy in general. Changes in body contour for instance can be assessed easily with 3D imaging. A retrospective analysis of Conebeam-CT (CBCT) images from the NKI showed the need of replanning at some point in the treatment course in 15% patients treated for lung cancer.

Besides monitoring patient position and anatomical changes, 3D imaging can also be used for QA goals. Questions regarding the positioning of the patient relative to their immobilisation devices can be investigated using 3D images; e.g. is the right knee-support used, or is the patient well positioned on the used belly board device? In some cases this might give us an explanation for unstable or incorrect patient positioning. Also, the quality of (individual) built-up materials and their application can be assessed.

With all these new possibilities the need for a systematic analysis of 3D images is born. We no longer can perform image registration in terms of translation and rotations only. Ideally, the acquired images should be analysed on changing anatomy and immunization qualities systematically, or at least at different moments during the treatment of the patient. Furthermore, we need to have a strategy on how to act when the anatomy no longer resembles the situation on the original reference CT-scan. A protocolised method for evaluating the effect of anatomical changes, e.g. by recalculating the actually given dose using the CBCT image, would be a necessity. But maybe the most challenging part is finding the time and resources to be able to truly utilize all benefits that volumetric imaging is offering us.

Patient reported outcomes versus clinical assessment of radiotherapy adverse effects

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Patient reported outcomes (PRO) are of increasing interest as measures of disease- and treatment-related outcomes after radiotherapy. They have long been accepted in the palliative setting, but it is only recently that a primary role in the curative setting has been investigated. This interest is stimulated, not only by the validity and reliability of PRO, but also by their relative ease of administration and collection.

PRO can be restricted to recording specific disease- and treatment-related symptoms or extended to include broader qualities such as emotional well-being, social and sexual functioning and overall satisfaction with life. Fully-validated multi-item questionnaires are available, including some that are not cancer specific (MOS SF36, EQ5D) and others that are cancer non-site specific (EORTC QLQ-C30), cancer site specific (EORTC QLQ-BR23) and treatment specific (FACT N, for neutropenic sepsis). The identification of questionnaire(s) appropriate for a specific clinical context is extremely important, and requires expert guidance. Assuming research questions are precisely defined and the appropriate PRO measures are fully incorporated in the analysis plan, questionnaires need to be administered to patients by trained staff with the time to explain how to respond to the questions. As with clinician assessments, >10% missing data present serious problems to analysis and interpretation, since reasons for missing data may be linked to the outcomes under study.

UK breast hypofractionated radiotherapy trials are among several studies that illustrate the potential power of PRO in research. PRO of breast shrinkage and hardness perform as well as change in photographic breast appearance scored by independent observers in discriminating small differences in randomised dose, and generate comparable estimates of α/β for endpoints such as change in breast size and hardness. This is despite limited concordance between clinician and self-assessments at the level of individual patients. Initial testing curative radiotherapy has yet abandoned clinical assessments of treatment outcome, this may be only a matter of time. Finally, although PRO and standard external assessments can function well as therapeutic endpoints, they do not necessarily distinguish between the different pathological processes (atrophy, fibrosis, telangiectasia etc), a requirement that may prove essential in correlative research into genetic susceptibilities.

Consensus on brachytherapy dose - volume parameters in 2013

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Traditionally, treatment planning in brachytherapy has been based upon 2D imaging and specific points have been used for prescription and reporting. With the introduction of image guided brachytherapy (IGBT) it has been possible to move from point prescription to pre-scription of dose to 3D target volume in terms of dose volume histogram parameters.

In radiotherapy in general it is essential to use a common language in order to compare clinical results from different centres worldwide. Applying IGBT it is important to use a terminology adjusted to the complex nature of such treatment technique. Preferably the same terminology should be used for different brachytherapy sites. It should also be harmonised, as far as possible, to the terminology used in external beam radiotherapy (EBRT), e.g. ICRU83.

Several recommendations on 3D image based treatment planning have been published for various brachytherapy sites the last ten years. In an upcoming ICRU/IGEC ESTRO recommendation for cervical cancer brachytherapy, concepts and terms for target and OAR definitions, biological dose modelling and DVH parameters are described for IGBT.