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Over the past years radiotherapy has undergone a substantial development that has led to improved outcome (both in terms of survival and toxicity) and widening of indications. This is mainly due to more advanced dose delivery techniques that allow performing curative treatments without exceeding normal tissues tolerance limits. These new developments cannot be fully exploited without an adequate imaging. The role of imaging is fundamental in several steps of modern high precision radiotherapy. Different imaging technologies are employed: to define volumes to be irradiated, to check patient positioning and to evaluate response to treatment. Volumes to be irradiated are defined according to ICRU reports. Traditionally morphologically pathological areas are considered. According to body site multiple imaging modalities can be used (e.g. CT and MR) and fused to better evaluate gross tumor volume (GTV). A potential improvement from the simple morphological approach can be achieved adding functional imaging (PET, perfusion/diffusion MR, spectroscopy) for GTV contouring. The concept of GTV can be extended to consider different sub-volumes that may have more aggressive behavior (Biological target volume or BTV). So far hypoxia has been the more extensively investigated parameter to define BTV. Hypoxia imaging is performed with PET employing dedicated radiotracers like 18F-MISO, 18F-FAZA or Cu-ATSM (several isotopes of copper can be employed with 60-Cu being the most common one). Hypoxia imaging has been shown to correlate with survival in head and neck and in gynecological cancers. Response to radiotherapy rarely result in a total disappearance of the neoplastic mass. Persistence of a fibrotic nodule is compatible with a positive result. Criteria usually employed to evaluate tumor response (RECIST criteria) were developed mainly in the setting of surgical and pharmacological treatments and consider all residual nodule as active disease. In clinical practice only long term stability of residual nodules can be considered a sure sign of their non active nature. Functional imaging can be used to anticipate this information investigating: changes in blood flow (perfusion MR and or CT) changes in cellularity and related water diffusivity (diffusion weighted MR), changes in predominant molecular content (MR spectroscopy) and changes in metabolism (PET with glucidic, aminoacidic, or nucleic acid tracers). Anticipation of response can be used in follow up but more interestingly can also be used during delivery of radiotherapy to fine tune the treatment with an adaptive approach. PET and spectroscopy have a spatial resolution limit that should be carefully considered if they are to be used in the setting of target volume definition. Moreover dedicated imaging devices (X-Ray, KV and MV cone beam CT, ultrasound) are more and more often used to check patient positioning in the framework of the so called image guided radiotherapy (IGRT).

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