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Inclusion of biological information in treatment plan optimization

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The response to radiation therapy is determined by a number of cellular, proliferative and tumor physiological factors. Recent development in molecular and functional imaging provides non-invasive information about these factors and can potentially be of value in treatment plan optimization. This represents a challenge to the central dogma in radiation therapy as a tailored, inhomogeneous dose is favored in stead of striving for a homogeneous dose to the target volume. One challenge is to develop optimization strategies that take the biological information of the tumor tissue adequately into account. A prerequisite for such strategies is detailed knowledge about the dose modifying factor (DMF) associated with the various biological features visualized by different imaging techniques. For most biological factors of relevance for the response to radiation therapy DMF is not well established. The dose modifying effect of tumor hypoxia, i.e. the oxygen enhancement ratio (OER) - has, however, been extensively studied. Moreover, dynamic contrast enhanced MR imaging and PET imaging with Cu-ATSM or F-Miso as traces have shown to be promising with respect to imaging of tumor hypoxia. Spatial redistribution of the dose according to hypoxia maps, derived from MRI or PET images, has shown to increase calculated tumor control probability (TCP) significantly compared to a homogeneous dose distribution in canine head and neck tumors. The effect depended on the degree of reoxygenation, with a maximum relative increase in TCP for tumours with poor or no reoxygenation. Also, acute hypoxia reduced TCP moderately, while underdosing chronic hypoxic cells gave large reductions in TCP. Random errors in positioning were found to give a small decrease in TCP, whereas systematic errors were found to reduce TCP substantially. Molecular and functional imaging provides vast amount of information and the strategies for incorporating this information into treatment plan optimization is still in its infancy.