Unlocking the therapeutic potential of X-ray triggered photodynamic therapy for lymph node metastasis treatment in rectal cancer models

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Rectal cancer has been a leading cause of cancer-related mortality worldwide. Local lymph node metastasis remains a critical challenge in rectal cancer management and seriously affects the treatment prognosis. This study is the first to assess the efficacy of X-ray triggerable photodynamic therapy (X-PDT) on metastatic lymph nodes in rectal cancer. The therapy uses a lipid-polymer hybrid nanoplatform loaded with verteporfin (VP) and conjugated with targeting molecules. Upon receiving a single 4 Gy fraction of X-ray radiation, VP was effectively activated, generating sufficient reactive oxygen species (ROS) to induce cancer cell death – however surrounding tissue was less affected and was spared. The efficacy of this strategy is demonstrated through in vitro cytotoxicity data in HCT116 cells, significant inhibition of primary tumour growth in both orthotopic and subcutaneous mouse models, and the suppression of lymph node metastasis progression in vivo. The findings indicate the possibility of a new and safe treatment for metastatic lymph nodes in deep tumours, paving the way for clinical translation of X-PDT.