Introduction

- Cancer caused more than 10 million deaths worldwide in 2018, according to the World Health Organization (WHO).
- WHO predicts this number will grow to almost 40 million in 2040 [1].
- Targeted Radionuclide Therapy (TRT) is a cancer treatment modality that uses a molecule labeled with a radionuclide to deliver damaging ionizing radiation to tumors [2].
- TRT presents several advantages when compared to conventional RT, such as localized tumor efficacy and tumor cell specificity [2].
- Tumors often display different types of heterogeneity at the time of treatment, which can be overlooked during treatment planning [3,4].
- Treatment techniques considering tumor heterogeneity, such as escalating dose or dose painting [5], still require further investigation for implementation in TRT [6,7].

Aims of the Study

- Ascertain if irradiating different phenotypes within a tumor mass with different radionuclides significantly impacts the dose distribution in the whole tumor.
- Study the dosimetric effect of each decay mode in each radionuclide on the tumor tissue and on healthy tissue.
- Investigate the feasibility (in terms of strategic dose delivery to different tumor phenotypes) of personalized TRT directed to the tumor phenotype.

Materials and Methods

- A tumor model with 4 distinguishable phenotypes (#1, #2, #3 and #4) was inserted into the right lung of the adult female reference phantom (AFP) of the International Commission on Radiological Protection (ICRP) 89 – Fig. 2.
- For all considered radionuclides (131I, 99mTc, 124I, 169Tb, and 177Lu), each decay mode (Auger, Internal Conversion (IC), beta, X-ray and gamma) was taken into account.
- S-value (dose per cumulated activity) was calculated in the tumor phenotypes and surrounding healthy tissue (i.e. right lung and breast) according to irradiation scenarios i) and ii), using the state-of-the-art Monte Carlo (MC) program PENEOLE.
- The configurations selected from the considered scenarios i) and ii), shown in Fig. 2, were studied according to two dosimetry parameter: 1. S-value in tumor tissues 2. Dose Efficiency (DE), ratio between S-value to tumor and to healthy tissue.

2 irradiation scenarios considered in Fig. 2:

i) Current Practice – all four tumor phenotypes irradiated by one radionuclide
ii) Ideal – each tumor phenotype irradiated by a different radionuclide

References

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Results and Discussion

Tumor phenotype - Radionuclide Combinations

- Fig. 1: Several studies have aimed to identify tumor phenotypes based on radionuclides methods, such as anatomical and functional imaging. Adapted from [5].

- 169Tb delivers the highest S-value to the tumor.
- 177Lu has the highest DE and lowest S-value to healthy tissues.
- Combinations C1 and C2 show improvement to the dosimetry parameters when compared to using only one radionuclide to irradiate the tumor.
- C3 and C4 may have appealing applications in theranostics (i.e. high S-value to tumor of 169Tb combined with imaging applications of 177Lu).

Dose contribution with 169Tb (highest dose to tumor configuration)

- Highest dose to tumor is achieved by β electrons (1 order of magnitude above other decays).
- X-ray and γ photons also contribute with a significant amount of absorbed dose to the tumor tissue (i.e. similar to Auger electrons).
- β and γ decays depict highest dose values for healthy tissues.

Conclusions

- Results from MC simulations show that irradiating the phenotypes in a heterogeneous tumor with different radionuclides can act as dose enhancement in the tumor, as well as minimize dose to the surrounding healthy tissues.

- Optimize TRT to the tumor phenotype
- Multi radionuclide irradiation
- Personalized TRT
- Increase TRT efficacy and success rate

Future Work

- Acquisition and segmentation of clinical (e.g. PET-CT) images. Development of patient-specific voxel phantom describing an individual patient anatomy.
- Calculation of dosimetric and biological effectiveness (i.e. DNA damage) in the patient-specific voxel phantom, using MC simulations.
- Determination of the optimal tumor configurations (i.e. radionuclide – tumor phenotype pairings) and respective effectiveness.
- Study the effect that non-homogeneous dose distribution in the tumor can have on the outcome of cancer treatment.

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