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# A Software App for Radiotherapy with In-situ Dose-painting using high Z nanoparticles

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## Abstract

The purpose of this work is to develop an user friendly and free-to-download application software that can be employed for modeling Radiotherapy with In-situ Dose-painting (RAID) using high-Z nanoparticles (HZNPs). The RAID APP is software program written in Matlab (Mathworks, Natick, MA, USA) based on deterministic code developed to simulate the space-time intra-tumor HZNPs biodistribution within the tumor, and the corresponding dose enhancement in response to low dose rate (LDR) brachytherapy of I-125, Pd-102, Cs-131 and kilovoltage x-rays such as 50 keV and 100 keV. Through the GUI of RAID APP, the user will be directed to different features to compute various parameters related to the dose enhancement and the biodistribution of NPs within high risk tumor sub-volumes. The software was developed as tool for research purposes with potential for subsequent development to guide dose-painting treatment planning using radiosensitizers such as gold (Au) and platinum (Pt).

### Keywords

Dose painting; dose enhancement; high atomic number nanoparticles

## I. Introduction

Recent work has highlighted radioatherapy application with in-situ dose-painting (RAID) with radiosensitizers as a potential new approach for sub-volume radiation boosting [1]. In this approach radiosenstizers like gold or platinum-based chemotherapy drugs can be loaded in radiotherapy (RT) biomaterial (e.g. brachytherapy spacers, fiducials or Mammosite balloon), with sustained control release after implantation over the duration of radiotherapy to boost dose to the tumor sub-volume, while minimizing dose to healthy tissue. Other studies have concluded that the use of high atomic number (Z) nanoparticles like gold nanoparticles as radiosensitizers during RT at keV energies leads to significant dose enhancement to the tumor [2][3][4][5][6][7][8]. In this study, a free-to-download RAID APP

Conflict of interest

There is no conflict of interest

was developed as tool for guiding further research towards development and potential translation of the RAID developed. The RAID APP is software with the capabilities to simulate intratumor biodistribution and corresponding dose-enhancement to tumor sub-volumes as a function of parameters such as nanoparticle size, and initial concentration.

Details of the calculations of intra-tumor biodistribution and corresponding dose-enhancement are described in detail in our recent publications [9] [10].

## II. Materilas and Methods

A high risk tumor sub-volume on the scale of a tumor voxel was modeled as a cube slab of size 10 μm ×10 μm ×10 μm encompassing a tumor cell of diameter 10 μm (figure1). As described in our recent study [9], the RAID APP employs an analytical method to compute nanoparticle (NP) diffusion based on Stokes-Enstein equation, and Fick's law. The nanoparticles diffusion within high risk sub volume of tumor depends on size and initial concentration of nanoparticles and can be computed for different times and distance from where the nanoparticles are released from the surface of the RT biomaterial.

Dose-boosting to the high risk volume was due to the interaction of the low energy radiotherapy photons with the nanoparticles which induces the emission of photoelectrons and Auger electrons to deposit their energy within the tumor sub-volume

Based on this, the dose enhancement effect (DEF) for each voxel was defined as ratio of the dose to tumor voxel with and without the high-Z nanoparticles (HZNPs) when exposed to kilovoltage photon energies.

The RAID APP code was written in Matlab (Mathwork, Natick, MA) based on deterministic methods. The graphical user interface (GUI) of the program allows user to simulate the space-time intra-tumor HZNPs bio-distribution and DEF within the tumor sub-volume. The RAID APP allows for dose-painting calculations for low dose rate (LDR) brachytherapy sources described in the AAPM Task Group 43 (I-125, Pd-102, Cs-131), and for kilovoltage x-ray 50 keV relevant for Accelerated Partial Breast Irradiation with Mammosite [11] and 100 keV (used by the Oraya Therapy [3]. The App currently allows selection of either gold or platinum nanoparticles with the latter useful for platinum-based chemotherapy drugs like cisplatin [10]

## III. Results

Through the main menu of RAID APP GUI, users can simulate the intratumor biodistribution at different times and distances as a function of nanoparticle size, type and initial concentration. Figure 2 illustrates the GUI. Mean-while, based on the intratumor biodistribution, the corresponding DEF can also be determined.

The RAID APP prompts user to select distances, size and composition of NP for any clinically relevant brachytherapy or kV energy source. In addition, the RAID APP offers a possibility to analyze and compare biodistribution of NP and its correspondent DEF for

different spectra. Figure 3 shows a sample plot of DEF versus the concentration for different nanoparticle sizes.

## IV. Discussion

The RAID APP provides an easy tool to perform simulation of HZNPs biodistribution and its related DEF. The RAID APP can serve as a useful tool for nanoparticle-aided radiotherapy research for different tumor sites. For example, the RAID APP could be used to simulate the biodistribution of HZNPs and the correspondent DEF as illustrated for prostate cancer (figure 4) and for accelerated partial breast irradiation (APBI) (figure 5).

The current release only covers LDR brachytherapy sources and low kilovoltage x-rays (50 keV, 100 Kev) when using gold and platinum nanoparticles. In the perspective, other radiation spectrum could be included such MV energy [12] and high dose rate (HDR) brachytherapy source [8]. Furthermore, the use of the high Z based nanoparticles could be extended to other material such as Gadolinium, as published in other work [13].

It should be mentioned that the current version of the APP is based on work described in our recent publication with a number of inherent assumptions, e.g. homogenous nanoparticle distribution within the tumor sub-volume. The App is currently being further developed to include more rigorous deterministic and Monte Carlo calculations that better incorporates such factors as heterogeneous distributions towards dose-painting treatment planning.

## V. Conclusion

The RAID APP is free executable application software downloadable at https://sites.google.com/site/brachyapps/. It can be employed as a research tool for nanoparticle-aided radiotherapy with potential for subsequent development to guide dose-painting treatment planning using high-z nano-particle for different LDR brachytherapy sources and low keV x-rays.

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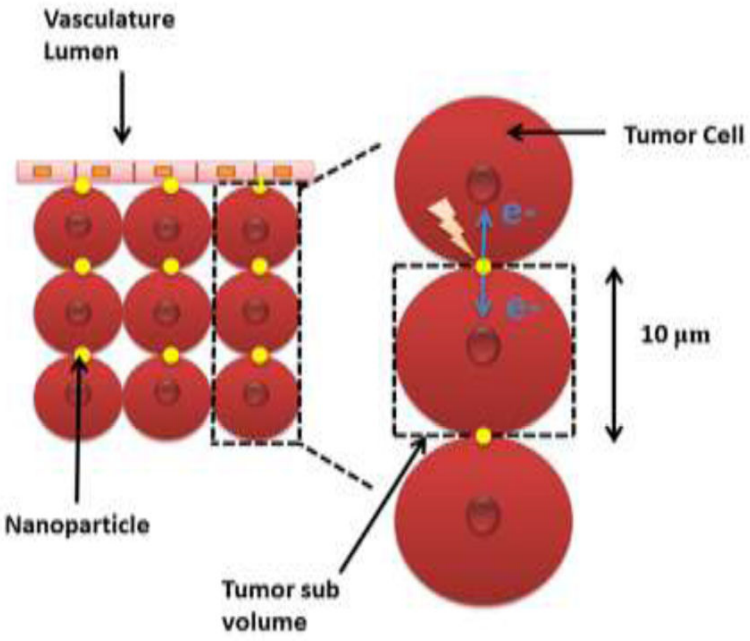


**Fig. 1.**
Model of tumor cell used to design the RAID APP

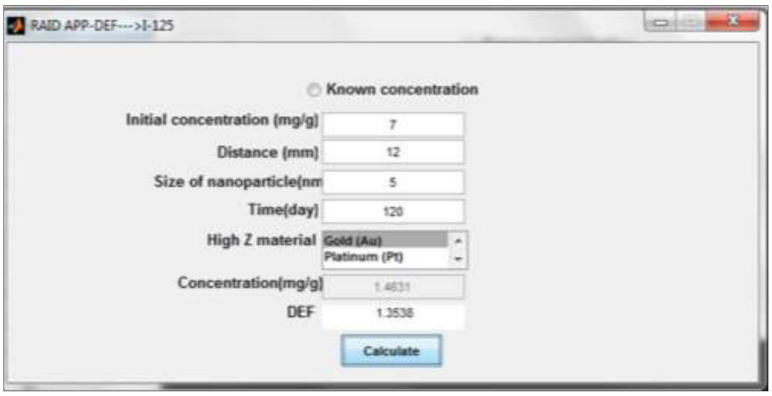


**Fig. 2.**

Example of GUI represents the simulation of diffusion time for I-125 and using gold nanoparticle

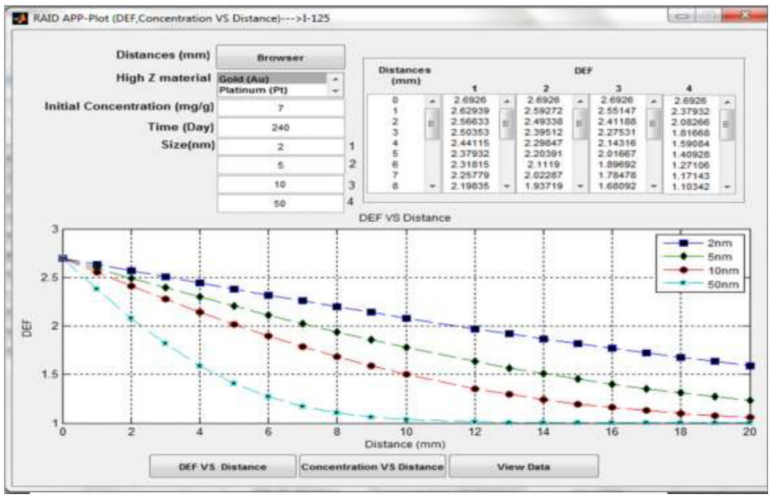


**Fig. 3.**

Example of GUI representing the plot of DEF VS Distance for I-125 using the gold nanoparticle

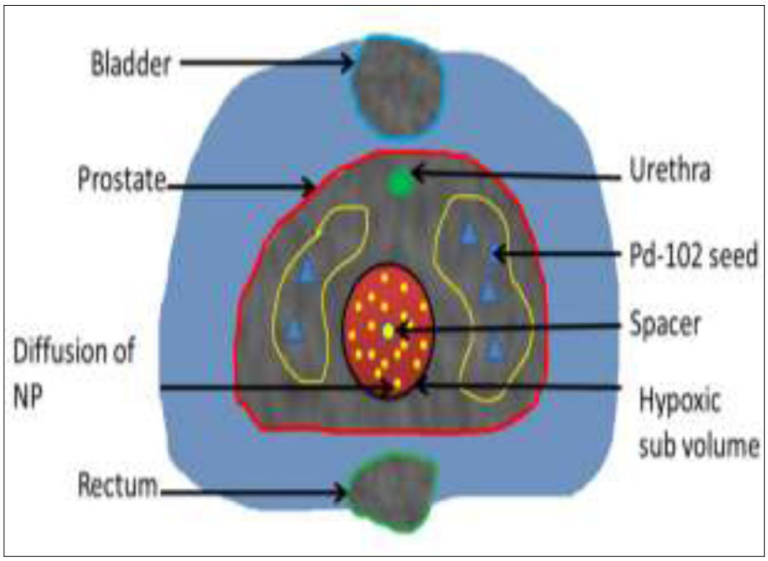


**Fig. 4.**

Some potential clinical application using RAID APP. With the presence of LDR Brachytherapy sources, the use of RAID APP to simulate a biodistribution of HZNPs and its related DEF for prostate cancer, in this case the spacer was coated

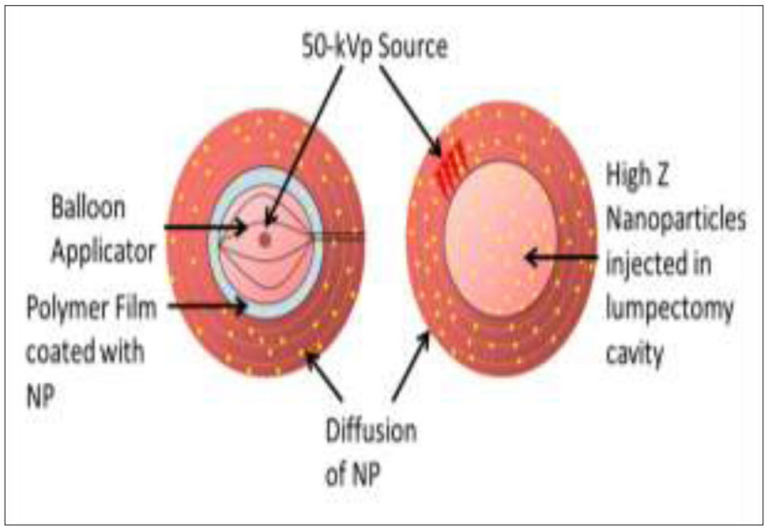


**Fig. 5.**

An other potential clinical application using RAID APP. With the presence of 50 kVp, the RAID APP could be used to simulate DEF and biodistribution of NPs for accelerated partial breast irradiation (APBI) using two approaches. First one, the spacer coated with polymer film containing the HZNPs. The second approach, the HZNPs was administered into lumpectomy cavity.