JULY 12–16 2020 VIRTUAL JOINT AAPM | COMP MEETING
EASTERN TIME [GMT-4]

Image-Guidance and Therapeutic Potential of Smart Radiotherapy Biomaterial and Titanium Dioxide in Pancreatic Cancer

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INTRODUCTION

- Titanium dioxide (titania, TiO_2) is a chemically inert, semiconducting material that also exhibits photocatalytic activity in the presence of light. Čerenkov radiation (CR) is light emission when charged particles travel faster than the phase velocity of light in a dielectic medium.
- Previous studies have shown TiO_2 nanoparticles predominantly cause adverse effects via induction of oxidative stress resulting in cell damage, genotoxicity, inflammation, immune response etc.
- After being excited by Cerenkov Radiation, titania forms electron-hole pairs and induces the production of reactive oxygen species (ROS).

AIM

To examine the efficacy of titanium dioxide (TiO_2) nanoparticles incorporated in a smart radiotherapy biomaterial (SRB_TiO_2) as a novel image contrast agent *in-vivo* and/or therapeutic agent for pancreatic cancer *in vitro* with/without radiotherapy.

METHOD

- **A colony forming assay *in vitro* was conducted using pancreatic cancer cells (KPC / Panc-02) treated with/without TiO_2 nanoparticles exposed to external beam radiotherapy.**
- **Smart radiotherapy biomaterials of TiO_2 (SRB_TiO_2) (3-5 mm length by 0.85-1.6mm diameter) were developed.**
- **Release of payload from the SRB_TiO_2 was investigated *in-vitro* without radiotherapy.**
- **Image contrast of SRB_TiO_2 was assessed using computed tomography.**

SRB_TiO2

Figure A. Pictorial view of SRB_TiO_2 Implants

RESULTS

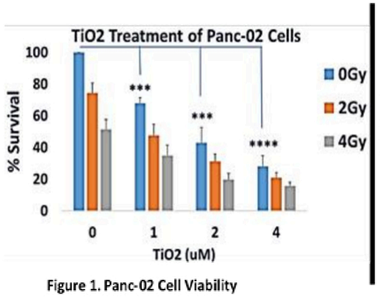

Figure 1. Panc-02 Cell Viability

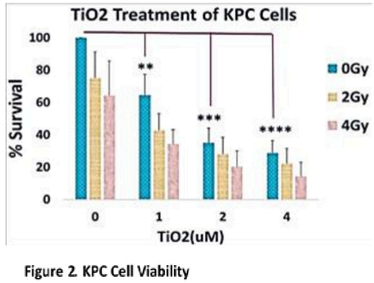

Figure 2. KPC Cell Viability

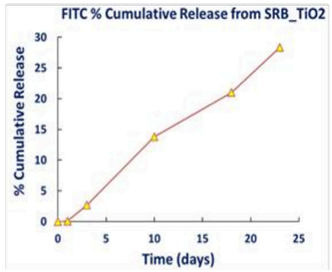

Figure 3. Cumulative Release of Fluorescein dye from SRB_TiO2 over Time

Figure 4. Pictorial view of SRB_TiO2 Implants

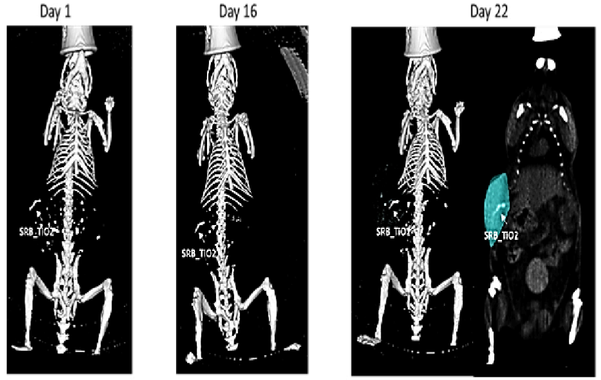

Figure [6] Computed Tomography images of Mouse with single KPC Tumor on the Left Flank implanted with SRB_TiO2 with no payload

Enhanced cytotoxic effects were observed for both KPC and Panc-02 cells treated with 1uM of TiO_2 nanoparticles exposed to 2Gy of radiotherapy. Sustained release of payload from SRB_TiO_2 was shown for up to 22 days. SRB_TiO_2 was clearly visible in CT images like fiducials for image-guided-radiotherapy (IGRT).

Figure 1 & 2 Cell viability results showed greater than 30% decrease in cell colony proliferation exposed to 1uM of TiO_2 nanoparticle without radiotherapy. With radiotherapy, significant decrease $p < 0.0001$ in cell viability for cells treated with 4uM at 4Gy of radiotherapy was observed. Figure 5 CT images of the SRB_TiO_2 in KPC tumor showed visible image of the implant 22 days post implant.

CONCLUSIONS

The results demonstrate the potential of next generation SRB_TiO_2 optimized for image-guided delivery of immunotherapy drugs in pancreatic tumors.

Radiotherapy beams produce Cerenkov Radiation within tissue, which has been widely studied recently for imaging purposes.

Furthermore, SRB_TiO_2 offer a viable pathway to clinical translation as they could simply replace currently used inert radiotherapy (RT) biomaterials (e.g. fiducials, beacons, spacers), at no additional inconvenience to many cancer patients like those with pancreatic, prostate, or lung cancer.

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ACKNOWLEDGEMENTS

- Brigham and Women's Hospital Biomedical Research Institute
- National Institutes of Health

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