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14. ABSTRACT
Clinical data show that there is a strong correlation between the cosmetic outcome of women with early stage breast cancers treated with MSB applicator and thespacing between the MammoSite balloon surface and the skin. Many women are not able to take advantage of MSB because of inadequate balloon-to-skin distances.The implementation of a thin customizable shielding layer to the MammoSite procedure will allow dynamic control over the skin dose overlying the MammoSiteballoon. Dose distribution may be monitored using a combination of methods that includes usage of a gamma camera detector system and scintillating fiber technology.Jefferson Lab's upgraded gamma camera system for BSGI may be used for imaging and dosimetric studies during IB. It will allow in real time verifying that breast skindose does not exceed the safety limits during the shielded MSB and hence also the shielding powder placement in the balloon implanted breast (phantom). Theobjective of this project is to develop innovative techniques and advanced technologies surround the IB methodology to facilitate more women taking advantage of APBIand therefore also of BCT to reduce breast cancer recurrence and increase survival expectancy. HU faculty and students will be integrally involved in research toadvance breast cancer treatment and improve patient outcomes collaborating with a national lab and a medical school gaining hands-on experience in movingtechnology form bench to bedside while building capabilities at HU to successfully compete for and conduct breast cancer research.

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Introduction

Hampton University (HU) is a historically black college (HBCU) located on Virginia's tidewater peninsula, about 10 miles from the Thomas Jefferson National Accelerator Facility (Jefferson Lab) and about 8 miles from the NASA Langley Research Center. The HU physics Department offers B.Sc, M.Sc, and PhD degrees in Physics with about 30 graduate students and 30 regular faculty in the department. This proposal will facilitate a collaborative research project with the research taking place largely at the nearby Thomas Jefferson National Accelerator Facility (Jefferson Lab or Jlab) initially, but later conveniently transferred to the HU Proton Therapy Institute (HUPTI). In the course of the collaboration, it is planned that HU researchers gain significant expertise in the high-end instrumentation-knowledge that will leveraged for future projects perhaps collaborative with Jlab and certainly competitive for mainstream funding support and sustainability research at the university.
The proposed project is an ideal choice for this model as it is crucially relevant for breast cancer care. It involves portable technology that can be initially developed at the Jlab site and then easily moved to and based at HUPTI. Strong clinical support is provided by EVMS, HUPTI. The close proximity of these three institutions with a history of working together ensures that HU researchers will have permanent access to resources otherwise inaccessible even to many large majority institutions. The Jlab resources include the detector and imaging group and laboratory an advanced machine shop staffed with expert technicians entire fast electronincs and data acquisition groups and a scientific computing center. With this level of support nearby, the development of a breast cancer instrumentation center at HU has a strong probability for success.

Body

HU faculty training for breast cancer research will spend a minimum of two full days /week routinely in the first two years working side by side on the proposed research projects with Jlab scientists. The proposed project has been carefully chosen to provide a wide range of skill training and a crucial knowledge base- all directly applicable to the development of breast cancer research at Hamtpton University. The project includes both diagnosis and treatment technologies, including: advanced imaging techniques, lesion localization, breast abnormality visualization, control and graphic software, surgical application and radiation oncology. Skills and expertise will be acquired in designing and building breast phantoms that allow the use of inflated brachytherapy applicator balloons to explore possible treatment protocols. HU personnel will also receive didactic instruction for usage of the microSelectron HDR High Dose Rate Afterloading System with an Ir-192 source for intracavitary brachytherapy procedures during laboratory pre-clinical imaging and dosimetry equipment testing, calibration and data processing, in collaboration with EVMS colleagues.

Mentees will obtain unique and transferable skills and expertise in: 1) novel approaches in advanced radiological modalities; 2) imaging system design and data acquisition software development for applications in nuclear medicine planar imaging and tomographic imaging; 3) electronics and detector instrumentation development; 4) breast phantom construction and implantation; 5) laboratory pre-clinical device testing calibration and data processing; 6) treatment planning algorithm development for intracavitary brachytherapy (IB); and 7) dose calculation approaches through image analysis

Key Research Accomplishments

Change in PI (from Keppel to Kenney) January 1, 2013

Aim 1 Evaluate the optimal powder arrangement, material and amount that are practical for reducing the skin dose. Data for detailed studies will be obtained utilizing relatively simple and equipment and precision Monte Carlo simulations.

Aim 2 Develop and test a practical method for application of a magnetic field for shield shaping. The method must be reproducible and provide the desired placement of shielding powders in the MammoSite balloon.

Aim 3 Develop an analytic model based on precision Monte Carlo simulations and laboratory data for determination of the required amount of powders to limit the skin dose to an optimal value deduced from several clinical trials.

Aim 4 Create an algorithm that uses the analytic model described in *Specific Aim 3* above, and provides as an output dose distribution in the treatment volume that is modified due to effect of the shielding. Modify an existing brachytherapy treatment planning program for MammoSite to incorporate this algorithm. Verify results with data.

Aim 5 Explore methods for determining the dose being delivered to the patient (breast phantom). Optimize dose monitoring via use of the gamma camera detector system, and scintillating fiber detector technology. Crosscheck these results against measurements with the MOSFET patient dose verification system to ensure accuracy and reproducibility.

1. **Starting January 1, 2013, from this award supported postdoctoral fellow, Dr. Lingyan Zhu has begun to contribute to some of the patient motion management/tracking research at the Hampton University Proton Therapy Institute. This research directly supports HUPTI's partial breast irradiation protocol at HUPTI, and so is in keeping with the goals of the grant.**

2. **Pre-PhD candidate John Okine (Department of Physics) has finalized his thesis and has begun manscript preparation. The following is summary of his findings during DoD support.**

ABSTRACT
Isodose lines of the enhanced dynamic wedge will be measured during commissioning of the enhanced dynamic wedge of the Varian 21EX Clinac at the DePaul Medical Centre using a dedicated plastic scintillator detector. The experimental setup consisted of 40cm x 40cm x 2cm plastic water phantom (CIRS Norfolk, VA), an array of 13, 0.1cm x 0.1cm x1.2cm scintillating fibers (BCF-60) each coupled to a 0.1cm x 0.1cm x 85cm light guide (BCF-98) with the aid of optical cement (EJ-500), a focusing lens (f = 25cm) and a charge coupled device camera (Alta U4000) that was connected to a computer for data analysis. The plastic water equivalence of the fibers was investigated using the Varian eclipse 10.0 treatment planning system. A plan was made for 6 MeV and a, 20cm _ 20cm field size for the 30o enhanced dynamic wedge. The fibers were found to be water equivalent since it showed to have the same Hounsfield unit as the plastic water. The plan shows a good isodose line distribution and percentage depth dose profile when compared to the physical wedge. With three different probing lengths of 3mm, 9mm and 20mm, the detectors response were investigated for dose linearity, dose rate constancy and field size effect. All three probing lengths of the detector were found to respond linearly and a close to flat response from 100 to 250MU and 300 to 600MU/min respectively. The 3mm and 9 mm probes gave almost constant dose, whiles the 20mm had a reduction of the dose when the field size was changing from 10x10cm to 35x35cm.

SPECIFIC AIMS
The purpose of this proposal is to measure the wedged isodose lines of the enhanced dynamic wedge on the Varian 21EX Clinac with a plastic scintillator fiber detector. The scintillator fiber detector measurement will then be compared to the ionization chamber in a water phantom measurement and Varian Eclipse 10.0 treatment planning system.

Aim 1. To verify the feasibility of the use of plastic fiber scintillator to measure the dose profile of the Varian enhanced dynamic wedge. Several devices such as the ionization chamber, diode, radiographic verification films and thermoluminescent dosimeters (TLD) but the scintillator fiber detectors have all been used to take dynamic wedge measurements. Each device has some advantage for one or more of the required measurement needed for the enhanced dynamic wedge implementation.

Aim 2. In order to achieve aim one, the limitation on size of the probing area of the detector for signal collection will be investigated. This will help to determine the probe size that will fit for the measurement of the EDW's dose gradient. It will also allow us to know the best size that will respond well to at least the lowest monitor unit as well as the highest monitor unit that will be encountered in the dose profile measurement.

Aim 3. Comparison of the signal subtraction technique to the chromatic extraction technique will be done. This will help us to know which of the techniques will give better dosimetric information. The dose signal subtraction technique will make use of a second fiber for Cerenkov subtraction whiles the color extraction technique will not.

RESULTS AND DISCUSSION

The water equivalency properties of the both the scintillating fiber and the light guide where tested. The coupled scintillator fiber to the light guide embedded in the solid water phantom was scanned under the CT scanner. This was done without spray-painting the fibers. A treatment plan was generated for 6 MeV and a, 20cm _ 20cm field size for the 300 enhanced dynamic wedge. The plastic water equivalence of the fibers when investigated using the Varian Eclipse 10.0 treatment planning system were found to be water equivalent since it showed to have the same Hounsfield unit for most part as the plastic water. There were some few small spikes long the Hounsfield unit profile but they are within acceptable limit to be considered to have a Hounsfield close to that of the plastic water. Figure 3 is showing the isodose distribution of the 20cm 20 cm field size, 300 enhanced dynamic wedge plan and its depth dose profile at a 5cm depth. The generated treatment plan also shows a good isodose line as well as percentage depth dose profile for the enhanced dynamic wedge used. The results will be compared to the results of the same investigation when the detector fiber is spray painted before CT scanning. If the spray paint does the dosimetric information will be distorted. A correction factor will be use to get the true dose information.

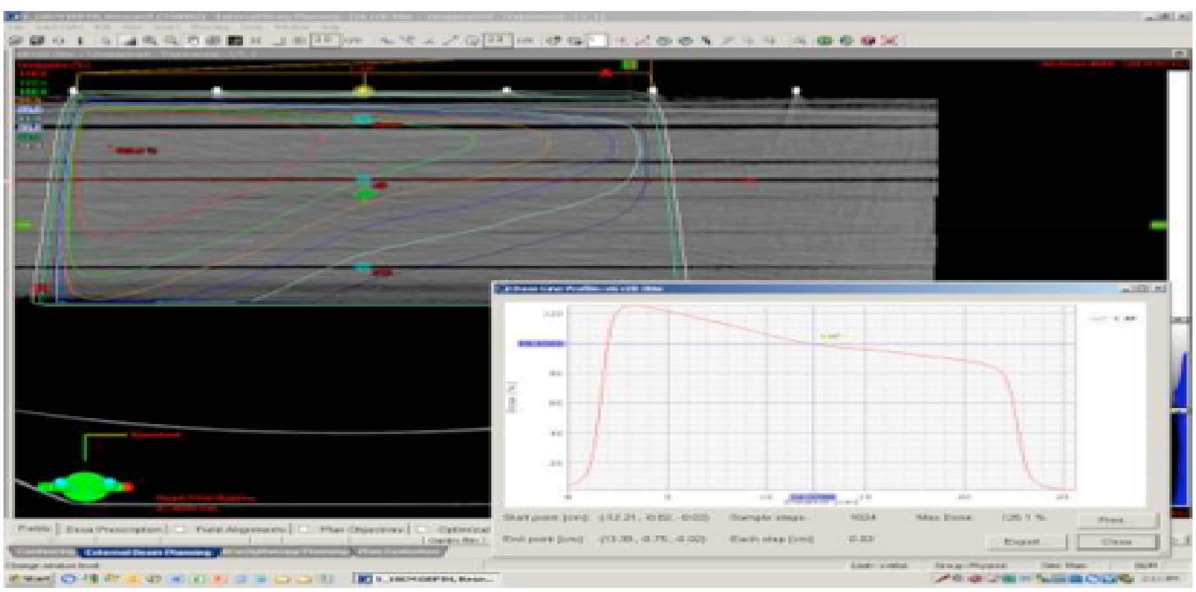

Figure 3. Depth dose profile of a 30^0 enhanced dynamic wedge plan

The limitation on size of the probing area of the detector for signal collection was investigated. This was done to determine the probe size and fit for the measurement of the EDW's dose gradient. The output of the three different sizes of scintillator fiber is displayed in figure 4. The goal here is to know the best size of probe that will respond well to at least the lowest monitor unit as well as the highest monitor unit that will be encountered in the dose profile measurement. Three different sizes of 3, 9 and 20mm long scintillator coupled to light guide was used. Each fiber has a light guide with no scintillator for the purpose of noise subtraction. As can be seen on the charge coupled device image on figure 4, the first image from left to right shows the weakest signal, whiles the second has the strongest signal and the third is intermediate due their brightness levels. The first, second and third images correspond to signals from the 3, 20 and 9mm scintillator respectively. From this, all three fibers are yielding an appreciable output at a 1.5cm depth (Dmax) when a 100MU of a 6MV energy photon was irradiated at a SSD of 98.5cm on to a 10 x 10 cm field size. The lowest and highest probable MU's encountered in enhanced dynamic wedge treatments will be irradiated to determine the optimal fiber size to be used for the detector.

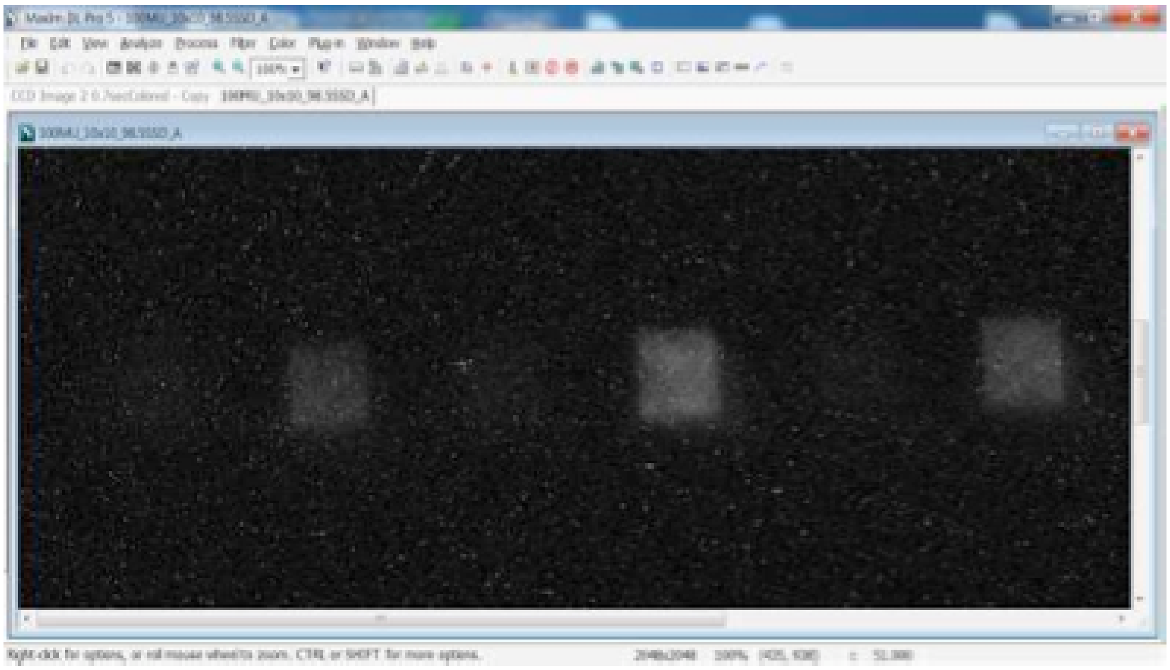

Figure 4. Output signal captured by the charge coupled device camera

As visualized in Figure 4 all three fibers responded well when detector was irradiated with 100MU of 6MV photons. The fibers signal strength increased when monitor units were increased by 50MU interval to 300MU which was evident on the images from the CCD camera. A plot of the various signal intensities from the different scintillator fibers sizes against the irradiated monitor unit was found to be linear. (shown in Figure 5A). As expected the intensities increased with increasing monitor units and the deviation from the fit is close to 1.The subtraction technique was used to take away Cerenkov noise from the signal. It can also be suggested the bigger scintillator fiber the more intensity compared to the smallest fiber. The dose rate constancy when investigated for a 250MU, was not flat as expected. As shown in Figure 5 B, there are fluctuations from the 20mm fiber signal. Apparently, both 3mm and 9mm fibers response are almost flat. In all the three fibers, the gradient of the fit was not zero, which is unexpected. We conclude that the fibers response is linear and the three different sizes have all given a good response. Finally, from these observations we suggest a detector with a good spatial resolution can be constructed by using either the 3mm or 9mm scintillator fiber. The subtraction method can be a vital tool in noise reduction. Our next set of experiments will be to compare chromatic extraction during the next signal analysis. We anticipate the fluctuation in dose constancy exhibited maybe a sign of coupling imperfection.

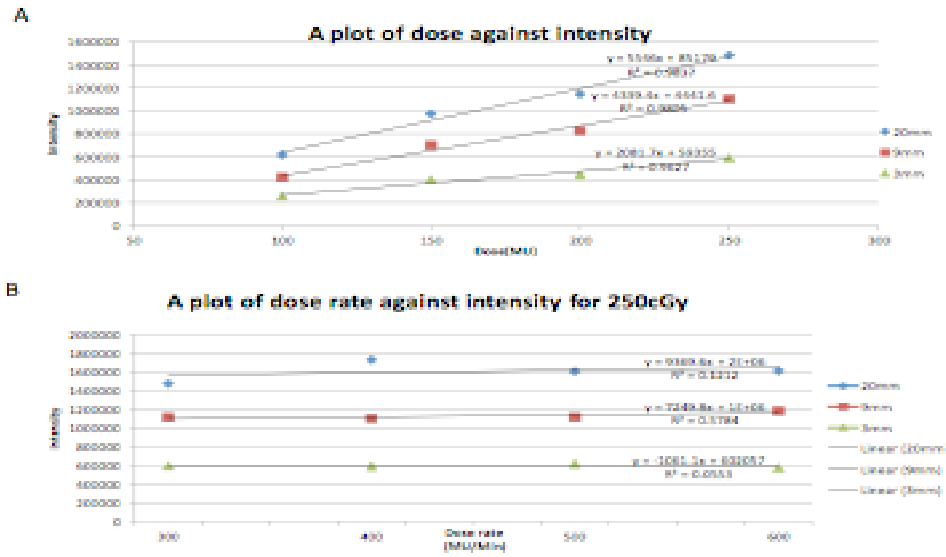

Figure 5. A. Linearity B. Dose rate constancy

Aim 6 Bench implement the entire procedure including treatment planning, powder insertion in balloon in phantom, magnetic filed application external to phantom and resulting dose measurement.

Aim 7 HU, Jefferson Lab, EVMS personnel will coordinate to expand the collaborative research endeavor to include additional breast cancer specific technology development projects.

Reportable Outcomes

1. We have finalized the subcontract to Jlab to begin the project "Apply SiPM technology developed for nuclear physics to improve breast cancer detection. The research goal is develop low profile gamma camera that would be used for breast cancer detection.

At HU: Provide capabilities and equipment to form the basis for continued breast cancer research with possibilities for future sponsored research support. This project will provide an opportunity for HU researchers and students to facilitate the development of an improved cancer imaging modality that could greatly improve patient care. The techniques and skills developed in working on this project could form the basis of a longer-term technology development or clinical implementation project, providing prototype data for future proposals and leading consequently to additional funding support.

At EVMS: Currently under university review. This project will provide an opportunity for HU researchers and students (**see John Okine's PhD thesis overview above**) to facilitate the development of an improved cancer imaging modality that could greatly improve patient care.

At JLab: This project will further develop and expand JLab's detector and imaging expertise particularly in the area of gamma imaging for cancer detection. In particular JLab will gain experience applying its high speed digitization technology and the latest silicon photo- multiplier technology to non-nuclear physics applications.

At: Dilon: Allow Dilon to make use of technical expertise and resources in Jefferson Lab and HU to facilitate the development of a SiPM based gamma camera which would have improved ability to detector breast cancer tumors. Development could lead to attracting additional funding to support construction of a clinical device leading to a new product for Dilon.

Tasks:
The following activities have begun

Jefferson Lab Tasks: The JLab Radiation Detector and Imaging Group will oversee the design and construction of a silicon photomulti- plier (SiPM) based breast cancer detector, mentoring an HU researcher also working on the project, and assist with detector calibration and breast phantom measurements to quantify the detector performance.

1. SiPM Gamma Camera Development. Jefferson Lab will design and construct the electronics necessary to produce a gamma camera able to fit in an existing Dilon camera body.
2. EFADC-16 Electronics Interface. Jefferson Lab will design and build circuitry to allow interfacing the SiPM channels of the SiPM gamma camera allowing for digitization with the JLab EFADC-16 digitization module.
3. Data Interface Software Development. Jefferson Lab will develop an API for Ethernet communication with EFADC,-16 data format, and calibration information. Jefferson Lab will assist Dilon with integration of the detector data into the Dilon software.
4. System Evaluation. Jefferson Lab will assist HU and Dilon with detector characterization as well as phantom and clinical evaluation of the system.
5. Report/Documentation Generation. Assist with the generation of technical (mechanical, electrical and software) documentation by the collaborating team regarding the operation and use of the SiPM based gamma camera. Jefferson Lab will work with the collaboration on the preparation of publications regarding the use of the system.

Dilon: Dilon Technologies will be responsible for detector evaluation and integration to the Dilon software.

1. SiPM Gamma Camera Development. Dilon will assist Jefferson Lab with the design construction of the SiPM detector to allow integration into a Dion camera body.
2. Data Interface Software Development. Dilon will assist with the design and testing of the API for Ethernet communication with EFADC,-16 data format, COG and calibration information. Dilon with Jefferson Lab will integrate he detector data into the Dilon system.
3. System Evaluation. Dilon will assist Jefferson Lab with the determination of the response function including calibration procedure. Additionally, Dilon will assist Jefferson Lab with phantom and clinical evaluation of the system.
4. Report/Documentation Generation. Dilon will direct the generation of technical (mechanical, electrical and software) documentation by the collaborating team regarding the operation and use of the Jefferson Lab handheld gamma camera. Dilon will work with the collaboration on the preparation of publications regarding the use of the system. HU: HU will be responsible for coordinating testing and evaluation of the system.

1. System Evaluation. HU will assist Dilon and Jefferson Lab with the determination of the response function including calibration pro-cedure, and with phantom and clinical evaluation of the system.
2. Scientific Analysis: HU will lead the analysis of the imaging results to quantify the performance comparison between the SiPM based detector and the Dilon 6800.
3. Report/Documentation Generation. HU will assist with the generation administrative and technical documentation by the collaborating team regarding the operation and use of the Jefferson Lab SiPM gamma camera. HU will work with Dilon and Jefferson Lab on the preparation of publications regarding the use of the system.

Conclusion

Thus far implementation of a thin customizable shielding layer to the MammoSite procedure has allowed dynamic control over the skin dose overlying the MammoSite balloon. Dose distribution can be monitored using a combination of methods that includes usage of a gamma camera detector system and scintillating fiber technology. HU faculty and one PhD candidate (John Okine) have been integrally involved in research to advance breast cancer treatment and improve patient outcomes collaborating with a national lab and a medical school and gaining hands-on experience in moving technology from bench to bedside while building capabilities at HU to successfully compete for and conduct breast cancer research.