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Real-Time *In Situ* Radiation Detection for Mitigating Injury to the Gastrointestinal Tract

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***Abstract*—Radiation therapy is a common cancer treatment method. However, injury to the gastrointestinal (GI) tract remains an unavoidable side effect, which reduces patient quality of life and increases healthcare costs. *In vivo* dosimetry is a treatment adaptation tool that helps reduce geometric setup uncertainties by providing real-time feedback on the patient's absorbed dose in the local body area where the technology is positioned. Current *in vivo* dosimetry technology is limited to measurements in minimally invasive areas of the body. This work demonstrates the use of PIN diode-based capsule electronics placed internal to the GI tract for increased precision radiation monitoring.**

The diode was first characterized *in vitro* for response to gamma and X-ray radiation and to varying temperatures ranging from 20 °C to 40 °C. Various sources were employed for characterization, including Cesium, Cobalt, 320 kV X-ray irradiator, a thermal neutron beam sourced by a 5.7 MW nuclear reactor, and a therapeutic linear accelerator (LINAC) with 6, 10, and 18 MV beam qualities. The diode was then placed in a swine's stomach to observe *in vivo* X-ray radiation detection.

The diode showed repeatability within 3% during its detection of the tested range of gamma and X-ray intensities and energies. The LINAC characterization results show the diode to be energy-independent for absorbed doses below 3.0 Gy. As expected, radiation absorption by body tissue greatly influenced the differing results between the *in vitro* and *in vivo* studies. This study demonstrates successful, first-time in situ radiation detection directly from core body areas in a non-invasive manner.

***Clinical relevance*— A real-time dosimeter, purposed for *in vivo* detection, has been characterized using pre-clinical and clinically used irradiators.**

***Index Terms*—gastrointestinal tract injury, radiation dosimeter, radiation therapy**

I. Introduction

Radiation therapy has been widely used to treat different types of cancer. However, acute and chronic radiation-induced injury to the gastrointestinal (GI) tract is often unavoidable. Radiation-induced injury reduces the patients' quality of life and creates an extra burden on healthcare costs [1].

Computed tomography (CT) simulation and dose-volume histograms are two common pre-treatment assessment methods used to guide radiation treatment planning to achieve the desired target coverage while mitigating radiation-induced toxicities to the healthy tissue. However, the success of the pre-treatment assessment methods heavily relies on the processes that compensate for organ movements, such as immobilizing patients in the same position as that of the CT simulation throughout the entire treatment, or the use of image-guided techniques that help correct for geometric fractional movement [2], [3]. There is a large degree of uncertainty in the delivered fractional dose received by localized regions due to geometric setup uncertainties and the variability of internal anatomy among treatments [4]. This remains a difficult feat to monitor with contemporary *in vivo* dosimetry techniques.

In vivo dosimetry is developed to bridge the gap to provide physicians with real-time feedback on treatment delivery errors, assist in treatment adaptation, and record the actual dose delivered to the patient. Modern *in vivo* dosimetry is limited to measuring doses in locations requiring minimal invasive placement, such as the skin. The accuracy is highly dependent on the placement relative to the treatment field applied to internal organs [5].

To address this unmet need for actual *in vivo* detection of radiation dose for mitigating GI injury, this work demonstrates the feasibility of using PIN diode-based capsule electronics to measure the dose directly in the GI tract. The capacity of real-time and *in situ* detection of radiation could mitigate GI injury by continuously monitoring GI doses during the therapy.

II. Methods

A silicon PIN photodiode (BPW 34 FS) was employed for *in vivo* radiation detection due to its compact size (4.3 x 4.3 mm), low power draw, and exceptional radiation sensitivity (active area of 2.65 x 2.65 mm). First, the photodiode's *in vitro* performance was characterized in terms of real-time detection

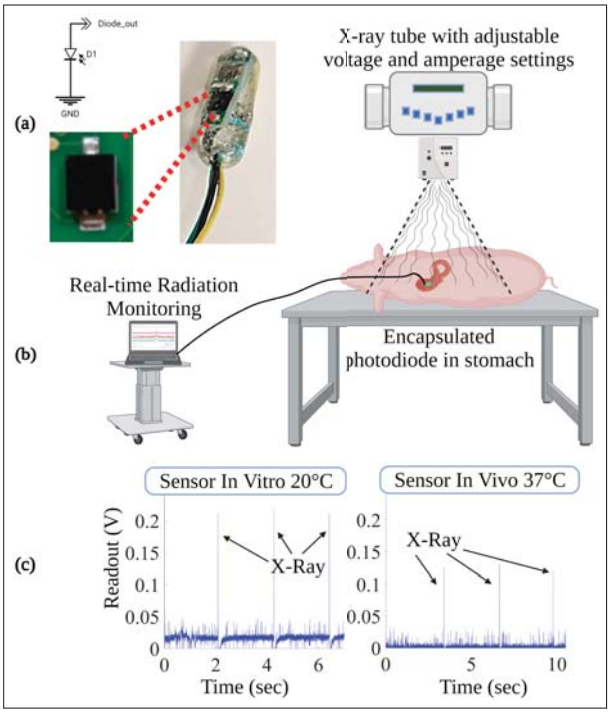

Fig. 1: (a) Optical images of the PIN photodiode and the encapsulated capsule electronics as well as the associated electrical schematic. (b) The schematics of the overall in vivo experimental setup. (c) In vitro (left) and in vivo (right) readouts of the PIN diode.

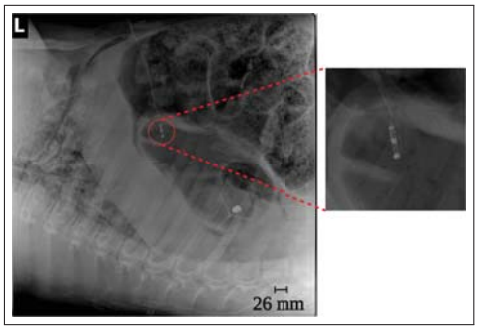

Fig. 2: X-ray image of the encapsulated PIN photodiode positioned within the stomach of a swine.

of gamma and X-ray radiation with varying temperatures ranging from 20 °C to 40 °C. A variety of radiation sources were employed for *in vitro* characterization, including Cesium, Cobalt, 320 kV X-ray irradiator, a thermal neutron beam sourced by a 5.7 MW nuclear reactor, and a therapeutic linear accelerator (LINAC) with 6, 10, and 18 MV beam qualities. Any ambient light was shielded by the setup for all *in vitro* tests. The diode and associated electronics remained wired to allow connection to a computer application, where the output voltage signal was monitored during the radiation exposure.

A. Pre-Clinical Research Irradiators

The Cesium and Cobalt sources were each housed in their respective irradiator machines. The Cesium irradiator (Best Theratronics, Ltd.) has a radiation field size of 527.2 cm^2 with a chamber height of 9.9 cm. An electric drive mechanism removes shielding from around the Cesium during operation. The Cobalt irradiator (Atomic Energy of Canada, Ltd.) has a radiation field size of 181.5 cm^2 with a chamber height of 20.6 cm. An electric drive mechanism lowers the chamber into the drum containing the Cobalt sources. The electric drive mechanisms operate at the same rate during each irradiation, contributing to a transition dose. The dose rates during the time of testing were 0.84 Gy/min and 28.53 Gy/min for Cesium and Cobalt, respectively. For the 320 kV, 12.50 mA X-ray irradiator (Precision X-Ray, Inc.), the sample is placed on an adjustable tray surface which sits directly under the X-ray tube within an irradiation chamber (75 x 86 x 102 cm). The tray can be positioned either 40 cm (3.75 Gy/min dose rate) or 50 cm (2.35 Gy/min dose rate) from the X-ray tube. The irradiation duration was adjusted such that the same dose was achieved from each source. The purpose of the irradiator tests was to observe the PIN diode's detection sensitivity and repeatability in the tested range of photon energies and intensities.

For each irradiator test, the diode is placed at the center of the tray or chamber, and the tray or chamber door is shut. The delivered radiation dose and time duration are based on a pre-programmed dose rate within the machine interface. Turning the machine on unshields the radiation source or begins X-ray generation. Automatically after the programmed time, the irradiator's source is shielded or the X-ray tube's power supply is shut off.

The nuclear reactor, which sourced the thermal neutron beam, is powered by the process of uranium fission and is maintained at 100% power (5.7 MW) as much as practical. The thermal neutron beam has filters in place to remove the majority of the fast neutron, epithermal neutron, and gamma radiation. The purpose of the neutron beam test is to observe the response and durability of the diode when bombarded by neutron particles. It was also desired to observe the diode's sensitivity to any present gamma radiation and to compare that output with the beam's calculated gamma dose rate and the irradiators' photon data.

For the thermal neutron beam tests, the diode was immobilized in the center of the holding tray (22 x 16 cm), and the tray was locked in place in the direct path of the beam's aperture in an enclosed area. The enclosed area was not accessible by personnel while the nuclear reactor was powered on. An operator remotely withdrew the appropriate mechanical and water shutters to allow a radiation flow path. The diode was irradiated at an initial temperature of 20 °C. The shutters were restored in place after the pre-determined irradiation time. Calculated dose rates were 0.2 Gy/min from gamma, 0.02 Gy/min from fast neutrons, 1.0×10^{-4} Gy/min (flux: 8.4×10^{4} to 2.6×10^{5} n/s/cm^2) from epithermal neutrons, and 1.5 Gy/min (flux: 1.5×10^{9} to 3.1×10^{9} n/s/cm^2) from thermal neutrons.

B. Clinical Irradiator

The LINAC (Elekta Versa HD) is primarily purposed to deliver precision X-rays for radiation treatment. In support of this study, the LINAC is used to characterize the diode for its

dose linearity, dose rate, and energy dependence. The diode is prepared for irradiation to mimic the setup that would be performed for a patient. The diode is centered at a depth of 10 cm within a water-filled phantom (30 x 30 x 30 cm) at 20 °C. The LINAC beam quality is set as 6, 10, or 18 MV. The source-to-skin distance (SSD) is adjusted to deliver the intended dose rate respective to the set X-ray energy. The diode is exposed to the X-rays until it absorbed a pre-determined total dose. For each beam quality and SSD combination, the diode is exposed to the same total dose.

C. In Vivo Study

In preparation for the *in vivo* study, the PIN diode was encapsulated in a standard 000 capsule (9.9 x 26 mm) together with a biocompatible epoxy to prevent electrical short circuits from gastric fluids. Further *in vitro* testing using the capsule electronics is performed with the 320 kV X-ray irradiator to observe temperature effects on the diode. To control environmental temperature, the capsule is submerged and secured in a 100 x 15 mm petri dish water bath. The petri dish is stationed on a heating plate, which remains in the irradiator during testing to aid in keeping constant conditions. The X-ray energy, dose rate, and total delivered dose remained constant with each irradiation. The heating plate temperature is increased from 20 °C to 40 °C in 5 °C increments, to represent the transition from room to body temperature, while recording the diode's readout.

All *in vivo* studies are approved by the Massachusetts Institute of Technology Committee on Animal Care. Four female Yorkshire swine (Animal Biotech Industries, Inc., Doylestown, PA, USA) in the range of 60–80 kg are used for the testing of the diode-based capsule electronics. X-rays (110 kV peak, 3.75 mA sec, 0.10 sec duration) purposed for diagnostic imaging is the radiation source. This X-ray source is not enclosed in an irradiator machine and instead delivers X-rays in an open room over an examination table as shown in Fig.1. For *in vitro* evaluation, the capsule is placed on the examination table, 95 cm from the X-ray tube, at 20 °C. Then, multiple X-rays are taken and the signal is recorded. For *in vivo* evaluation, the swine are sedated and anesthetized using Telazol (5 mg/kg) and Xylazine (2 mg/kg). The capsule is then endoscopically placed in the stomach of each of the four swine on different occasions. The swine are placed on the examination table in a recumbent position such that the stomach is directly under the X-ray tube. Based on the size and anatomy of the swine, the capsule is roughly 80 cm to 85 cm from the X-ray tube. The capsule electronics remained wired throughout all studies, which held the capsule stationary in the stomach. Multiple X-rays are taken of the swines' abdominal region to observe *in vivo* response.

III. Results

Fig. 1 demonstrates the difference in the X-ray amplitudes between *in vitro* and *in vivo*. The pulses in the plots and the bar graph values represent the received radiation doses on the skin and in the stomach while taking X-ray images. Fig. 2 shows one of the corresponding X-Ray images of the radiation detector in the stomach. Fig. 3 shows the photodiode's response to a non-uniformly distributed in vitro 110 kV peak X-ray field with varying distances to the radiation source and radiation intensities. Fig. 4 portrays the linearity of the photodiode's response when exposed to LINAC X-Rays of three different peak voltages for doses up to 3.0 Gy. The performance in the detection of the various gamma-ray sources and the therapeutic neutron beam is shown in Fig.5. Fig. 6 highlights the temperature effect on the photodiode's radiation detection performance at room temperature versus body temperature.

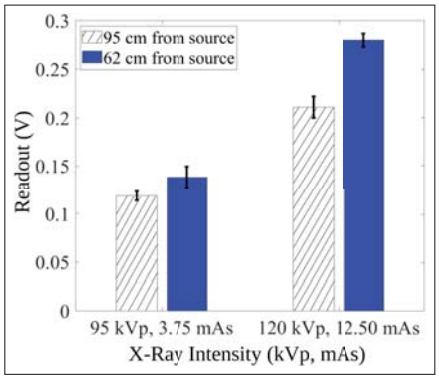

Fig. 3: Results from in vitro tests at 20 °C using the X-ray source also used for the in vivo testing. For constant X-ray intensity, reduced distance to the source increases the density of X-rays present, correlating to an increase in the radiation dose absorbed by the photodiode.

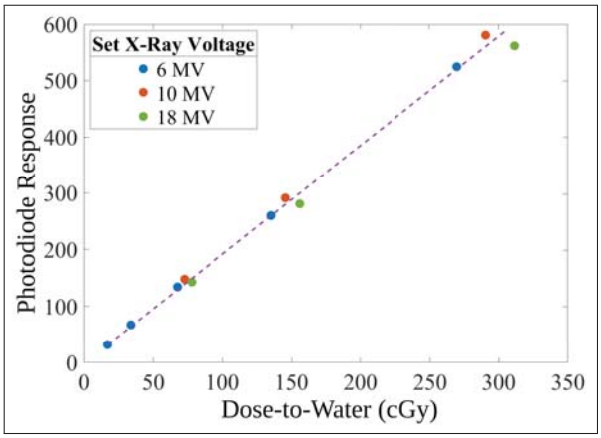

Fig. 4: Photodiode characterization using a LINAC to verify its reliability and consistency in detecting X-rays of varying intensities and energies. The photodiode response indicates the integral of the resultant pulse for the duration of irradiation. The dose-to-water represents the X-ray dose delivered to the photodiode regarding the set X-ray voltage.

IV. Discussion

The comparison of the *in vivo* and *in vitro* results using the same X-ray source and radiation delivery conditions highlighted the impact of environmental temperature and tissue

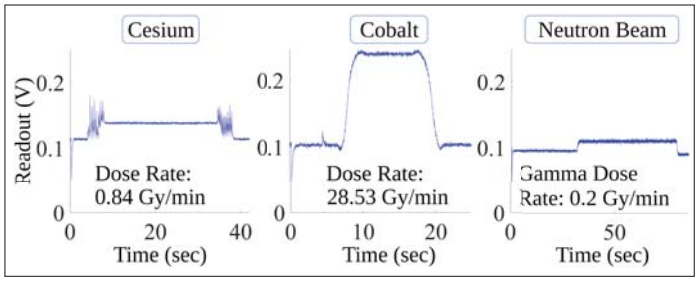

Fig. 5: The PIN photodiode displayed consistent gamma radiation detection from Cesium (2525 Ci), Cobalt (2100 Ci), and a neutron beam (5.7 MW nuclear reactor).

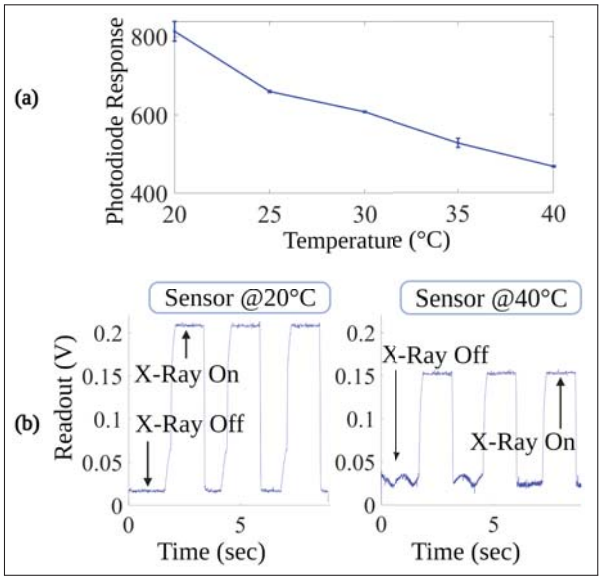

Fig. 6: (a) For constant X-ray exposure, the photodiode output voltage decreases steadily with increasing temperature. The photodiode response indicates the integral of the resultant pulse for the duration of irradiation. (b) Raw output voltages at 20 °C and 40 °C, two inputs of plot (a).

surrounding the diode during radiation exposure. For constant X-ray intensity and constant distance from the X-ray tube, the transition from *in vitro* at 20 °C to *in vitro* at 37 °C resulted in about a 20% decrease in diode output voltage due to the diode's negative temperature coefficient of voltage. While the diode's output voltage dropped 30% from *in vitro* conditions at 37 °C to *in vivo* conditions in the stomach due to radiation absorption in surrounding tissues.

As predicted, we observe that shorter distance from the X-ray source and higher X-ray intensity (penetration strength and number of particles) create a higher pulse height response in the diode. Particularly, the effect of increased intensity is magnified by reduced distance from the X-ray tube. For the same increase in X-ray intensity, the diode's pulse height readout increased about 40% at 95 cm compared to a roughly 50% increase at 62 cm from the X-ray tube.

When the same total dose is delivered to the diode via varying LINAC beam qualities, the diode's response remains linear, indicating energy independence. Energy independence reflects the dose and energy range that do not require further conversions to standardize the data. The diode response on the y-axis represents the background-subtracted integral of the output pulse for the duration of X-ray exposure.

During gamma radiation detection from the Cesium, Cobalt, and thermal neutron beam sources, the jump in pulse height represents the gamma rays being generated and absorbed by the diode. Only one irradiation trial from each source is shown, however, the trials not shown portray near-identical results. The diode showed reliability and dose repeatability within 3%. The pulse amplitude is observed to change as a function of dose rate, and the integral of the overall pulse is observed to change as a function of the total absorbed dose.

To compare results from the 320 kV X-ray irradiator tests observing the impact of temperature, the background-subtracted pulse integral value was calculated for each irradiation, and all integral values were averaged for each temperature. The averages and standard deviations were compiled in Fig.5(a). For constant X-ray intensity and duration, the diode's pulse amplitude decreases steadily with increasing temperature. This is in part due to the diode having a negative temperature coefficient of voltage, and it having the property of an exponentially increasing dark current with an increasing temperature above 0 °C.

V. Conclusion

The advent of ingestible *in vivo* dosimetry validates treatment planning and reduces dose discrepancies by monitoring radiation dose from near or within the organ of concern. This study successfully demonstrates the first-time in situ detection of radiation at core body areas via capsule-like electronics in a non-invasive manner. The capacity of real-time *in situ* tracking radiation provides physicians with real-time feedback on the received dose in the GI tract to actively monitor GI doses and improve therapy outcomes.

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