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In vivo dosimetry with optically stimulated dosimeters and RTQA2 radiochromic film for intraoperative radiotherapy of the breast

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Purpose: Measurements were taken with optically stimulated luminescence dosimeters (OSLDs) and with RTQA2 radiochromic film to evaluate the use of each for *in vivo* dosimetry with intraoperative radiotherapy of the breast.
Methods: Nonlinear calibration curves were established for OSLDs and RTQA2 radiochromic film using the Intrabeam 50 kV_p source. Measurements were taken in a water phantom and compared to absolute dose measurements taken with an ionization chamber to investigate the characteristics of both types of dosimeters, including energy response and radiative absorption. *In vivo* readings were taken on the skin and in the tumor cavity using OSLDs and RTQA2 radiochromic film for 10 patients and 20 patients respectively. A prescription of 20 Gy to the surface of the applicator was used for all *in vivo* measurements in this study.
Results: OSLDs were found to have an approximate uncertainty of ±7% for readings near the surface of the applicator and ±17% for readings at distances typical to the skin. The radiative absorption by OSLD was negative, indicating that this type of dosimeter absorbs less radiation than water in the targeted intraoperative radiotherapy energy range. RTQA2 film exhibited no energy dependence and all film readings were within ±8% of the delivered dose. The maximum radiative absorption in film was 8.5%. Radiochromic film measurements were found to be on average 18.2 ± 3.3 Gy for the tumor cavity and 2.1 ± 0.8 Gy for positions on the skin superior and inferior to the Intrabeam applicator. Average cavity measurements taken with OSLDs were 15.9 ± 3.9 Gy and average skin doses were 1.4 ± 0.8 Gy.
Conclusions: OSLDs produce results with an uncertainty comparable to other dosimeters near the surface of the applicator but the uncertainty increases to an unacceptably high level with distance from the applicator. RTQA2 radiochromic film is shown to be accurate both at the surface of the applicator and at distances of 1–2 cm. [http://dx.doi.org/10.1118/1.4819825]

Key words: intraoperative radiotherapy, dosimetry, optically stimulated luminescence

1. INTRODUCTION

Radiotherapy is a common treatment modality for patients diagnosed with breast cancer. Whole breast external beam radiotherapy (EBRT) is typically prescribed for 3–6 weeks. An attractive alternative to EBRT is intraoperative radiotherapy (IORT). Using the TARGeted Intraoperative radiotherapy (TARGIT) technique, treatment is delivered during the surgical procedure and can be completed in 30 min to an hour.

TARGIT makes use of a small x-ray source called the Intrabeam (Carl Zeiss, Oberkochen, Germany). Tumor is excised from the breast and a polyetherimide spherical applicator, of comparable size to the tumor, is selected. The source is attached to a robotic arm, the applicator is then placed over the Intrabeam source, and the source and applicator are inserted into the tumor cavity. A purse-string stitch technique is used to ensure conformity of the tissue against the applicator so that the shape of the tumor cavity matches the spherical dose distribution produced by the Intrabeam source. A standard prescription dose of 20 Gy to the surface of the applicator is then delivered over 15–40 min depending on applicator size.

An international randomized trial was launched in March of 2000 to compare the TARGIT approach with conventional EBRT given over 3–6 weeks. The difference between local recurrence rates at 4 years in EBRT and TARGIT was found to be 0.25%.[1]

In vivo dosimetry is an established method of verifying accurate delivery of radiation and identifying potential errors.[2,3] It is desirable in TARGIT to have a system in place that confirms accurate delivery of the prescribed dose and monitors skin dose to the patients. Various dosimeters have been investigated for use as *in vivo* dosimeters with TARGIT including radiochromic film and thermoluminescence dosimeters (TLDs).[4,5] Potential candidates for *in vivo* dosimetry of TARGIT procedures are optically stimulated luminescence dosimeters (OSLDs) and RTQA2 radiochromic film. To the best of our knowledge these dosimeters have not been used for *in vivo* dosimetry with TARGIT.

OSLDs have characteristics that are desirable for use in intraoperative radiotherapy procedures. The nanoDot OSLD produced by Landauer (Landauer, Inc., Glenwood, IL) measures 1 cm in width and height and 2 mm in thickness. The small size allows it to be placed easily on the patient's skin

close to the applicator and in the tumor cavity without undo disturbance to the surgical site. Steep dose gradients produced by the Intrabeam also indicate the use of a small dosimeter. OSLDs can be calibrated for use with low energy x-rays such as those used in the TARGIT technique.[6]

EBT2 radiochromic film has previously been investigated for use in acquiring *in vivo* measurements with TARGIT.[4] Radiochromic film is thin (0.5 mm) and can be cut to sizes that do not interfere with the delivery of intraoperative radiotherapy. It also does not require processing, reducing the cost and complex handling associated with silver halide film dosimetry. RTQA2 film was investigated for use with TARGIT in this study because it is commonly used for routine quality assurance checks with linear particle accelerators and is readily available in many radiation oncology departments.

This study investigated the characteristics of OSLDs and RTQA2 film to evaluate their use in *in vivo* dosimetric readings. Experiments were designed to evaluate the response of these dosimeters to the photon energy range and the doses typical to TARGIT. The absorption of both OSLDs and RTQA2 film was also investigated. *In vivo* measurements were taken in the tumor cavity and on the patient's skin at positions superior and inferior to the applicator. These results are reported and compared to the results of previously published works.

2. METHODS AND MATERIALS

Intraoperative breast treatment is performed at our center using the Intrabeam system from Carl Zeiss Meditec. The Intrabeam is a small, lightweight source that produces 50 kV_p x-rays. The x-rays are created by accelerating electrons and directing them down a needle-like probe that serves as a drift tube. The electrons strike a thin gold target located at the tip of the probe producing a spectrum of energies comprised of bremsstrahlung radiation and characteristic x-rays. The probe is 10 cm in length and 3.2 mm in diameter. The dose distribution produced is largely isotropic.[7]

Each procedure begins with a tumor excision. Once the tumor has been removed an applicator of appropriate size is chosen that approximates the size of the tumor. The applicators are spherical in shape to match the isotropic dose distribution. The applicator provides a surface for the tissue to conform to when pulled tightly against it. A typical applicator set ranges in diameter size from 3.0 to 5.0 cm in 0.5 cm increments. The applicator is placed over the needle-like probe of the Intrabeam source which is then attached to a robotic arm. The robotic arm allows the surgeon to precisely place the applicator and x-ray source in the tumor cavity where it will remain during treatment. The surgeon then uses a purse-string stitch technique to conform the breast tissue to the applicator. Adequate conformance is confirmed using real time ultrasound. The skin is then retracted from the applicator using a Lone Star Retractor ring and hook system (CooperSurgical, Inc., Trumbell, CT). The applicator size, prescription, and treatment depth from applicator surface are input into the treatment planning workstation so that the treatment time can be calculated. A treatment is then delivered.

A rigorous quality assurance program is in place for the Intrabeam system. The absolute calibration is performed at the factory and is confirmed onsite using a water phantom provided by Carl Zeiss Meditec along with a calibrated soft x-ray chamber model number 34013 from PTW (PTW, Freiburg, Germany). The energy response for this chamber is reported to be ±2% by the manufacturer. Before each procedure further checks are performed to confirm the isotropy and dose rate. These pre-treatment quality assurance checks have been previously described in the literature.[8]

In vivo dosimetry in this study was performed by placing the dosimeters, whether OSLDs or film, on the patient's skin at positions superior and inferior to the applicator. Skin dosimeters were placed under the Lone Star Retractor so that they were in contact with the skin surface. A third dosimeter was placed in the tumor cavity before the applicator was inserted. Sterile conditions were achieved by placing the dosimeters between two sterile Tegaderm dressings (3M, St. Paul, MN). The Tegaderm has a sticky surface and the dosimeters can be effectively sealed between two sheets of Tegaderm, a process which is affectionately called "making ravioli". It is noteworthy to mention that the process of removing the dosimeter from the Tegaderm can be greatly facilitated by placing the dosimeters in a small plastic bag and then sealing the bag in the Tegaderm. The dosimeter can later be cut out of the bag using scissors; otherwise the Tegaderm has to be peeled off of the dosimeter before reading.

After the procedure, dosimeters were recovered and read. The OSLDs used in this study were nanoDots by Landauer (Landauer,Inc., Glenwood, IL). The OSLDs were read using the Landauer MicroStar Inlight reader. Film dosimetry was performed using RTQA2 radiochromic film scanned with an Epson Perfection V750 Pro flatbed scanner in reflective scan mode and evaluated with OmniPro-ImRT software from IBA Dosimetry (Schwarzenbruck, Germany).

2.A. Calibration of OSLDs

OSLD dosimeters have been shown to over-respond to x-rays in the diagnostic energy range by a factor of approximately 3–4.[6] It is therefore necessary to generate separate calibrations for applications in the diagnostic energy range and in the therapeutic energy range. It has also been demonstrated that the response of OSLD dosimeters is supralinear above 2 Gy.[9]

A nonlinear calibration was established in order to create a calibration derived from measurements taken that span the range of expected dose readings and account for the supralinear response of OSLD dosimeters above 2 Gy. The Intrabeam itself was used to collect calibration data in this dose range. The experimental setup is shown in Fig. 1. Three OSLDs were taped to the applicator and placed in a water phantom to simulate treatment conditions. Doses of 0, 1, 2, 5, 10, 20, and 25 Gy were delivered to each set of three OSLDs using the Intrabeam source with the 4 cm applicator. The readings were used to establish a nonlinear calibration curve based on fitting the calibration data to the second order polynomial shown

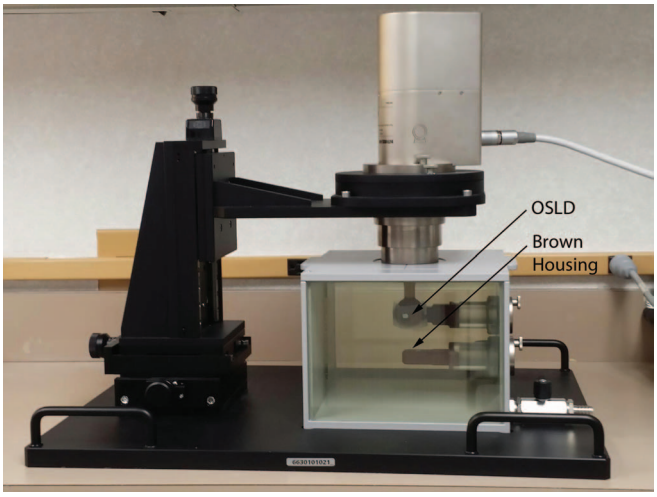

FIG. 1. Experimental setup for calibrating OSLDs in the water phantom.

in Eq. (1):

$$y = ax^2 + bx + c, \quad (1)$$

where x is the photon counts and y is the computed dose. The coefficients a, b, and c have units of dose/counts^2, dose/counts, and dose, respectively.[10] The intrinsic uncertainty of the system and calibrations was confirmed to be less than 2% using the method recommended by the manufacturer.[6]

2.B. Energy response of OSLDs

OSLDs have been reported to display energy dependence at diagnostic energies.[11] It is therefore necessary to determine the uncertainty associated with using dosimeters that do not have a flat response over the beam qualities found in TARGIT. The spectral shift due to beam hardening produced by various applicators and depths in tissue has been previously studied.[4] The effective energy of the beam in TARGIT was shown to range from 20.7 to 36.3 keV.

To characterize the change in response of readings taken with OSLDs due to the change in effective energy as a result of applicator size, readings were taken in a water phantom at a distance of 0.15 cm from the surface of the 3.0 and 5.0 cm applicators for doses of 15, 20, and 25 Gy. These doses were chosen because they cover the range of expected dose to the surface of the applicator in TARGIT. The treatment time necessary to deliver the doses was calculated from an absolute dose rate measurement in water using a calibrated soft x-ray chamber model number 34013 from PTW and following the procedure described in the Intrabeam Water Phantom User Manual.[12] Dose was delivered to the ionization chamber using the calculated treatment times. The 3.0 and 5.0 cm applicators were chosen because they represent the two extremes of the change in effective energy in TARGIT. It was necessary to take readings at a distance of 0.15 cm because this is the smallest distance from the applicator at which a 34013 PTW ionization chamber can be placed due to the need to waterproof the chamber. The experimental setup for irradiating the OSLDs involved securing the dosimeter to the surface of the brown housing of the water phantom shown in Fig. 1, adjusting the distance from the surface of the applicator to the surface of the OSLD to a distance of 0.15 cm, and delivering radiation for the calculated time. The brown housing serves as waterproofing for the ionization chamber and is made of solid water that is 0.1 cm in thickness. The nonlinear 50 kV_p calibration was applied to all the readings taken to evaluate OSLD response.

The OSLDs were also tested at various depths that correspond to typical distances between the applicator surface and the skin. The OSLDs were taped to the surface of the brown housing in the water phantom shown in Fig. 1. The distance between the surface of the applicator and the surface of the OSLD was then carefully set. Doses of 1, 3, and 5 Gy were delivered to OSLDs at depths of 1 and 2 cm. The 3 and 5 cm applicators were again used to represent the extremes of the effective energy in TARGIT. The nonlinear 50 kV_p calibration was applied to all readings. The differences in the resulting doses were used in determining the uncertainty associated with readings taken at typical skin to applicator distances.

2.C. Absorption in OSLDs

Since the OSLDs are being placed between the applicator and the breast tissue being treated, it is important to measure the x-ray absorption to facilitate a clinician's decision to perform *in vivo* dosimetry using this type of detector. To measure absorption, OSLDs were secured in the water phantom on the surface of the brown housing. A 34013 PTW ionization chamber was placed in a holder in the brown housing with the OSLD completely covering the active volume of the chamber at a point 0.15 cm from the effective point of measurement of the ionization chamber. Readings were taken for a fixed irradiation time of 1 min with the bare needle tip of the Intrabeam placed at distances of 0.5, 1.0, 1.5, and 2.0 cm from the effective point of measurement of the ionization chamber. Three readings were taken at each distance and the results averaged. The measurements were repeated without the OSLD and the resulting absorption was calculated.

An OSLD was also disassembled for the purpose of quantifying the absorption through the individual components of the dosimeter. The nanoDot dosimeter is composed of a plastic disk infused with aluminum oxide doped with carbon (Al_2O_3:C) encased in a plastic case.[13] The plastic case is composed of two virtually identical plastic pieces. The procedure outlined above was repeated with the front half of the plastic case and with the aluminum oxide infused plastic disk with the bare needle tip at a distance of 1 cm from the effective point of measurement of the ionization chamber and the resulting absorption was calculated.

2.D. Calibration of the radiochromic film

RTQA2 radiochromic film was also used to acquire both surface dose readings and readings in the tumor cavity. The film was calibrated with the Intrabeam using the same experimental setup as the OSLDs shown in Fig. 1. Films were taped

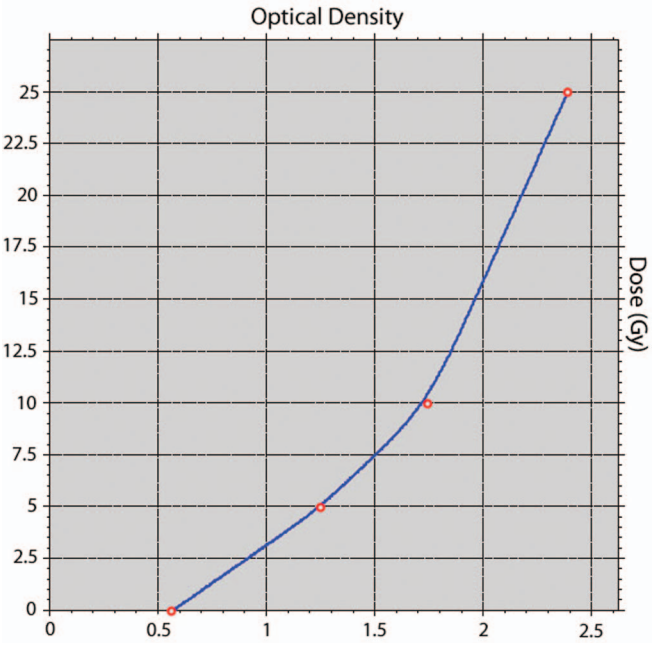

FIG. 2. Radiochromic film calibration curve.

to an applicator that was then placed in a water phantom. The films were exposed to doses of 0, 5, 10, and 25 Gy. The films were scanned on an Epson Perfection V750 Pro flatbed scanner. An interval of no less than 24 h was allowed between exposure and scanning to allow the films sufficient time to stabilize. The Epson Scan version 3.81US software was used to scan the calibration films using the following settings; Document Type: Reflective, Image Type: 16-bit Grayscale, Resolution: 50 dpi, and "No Color Correction." The scans were saved in the tagged image file format.

The scans were imported into OmniPro ImRT software and used to create the calibration curve shown in Fig. 2. Because the film could not perfectly conform to the surface of the applicator, the entire exposed area did not receive the same dose. Therefore an average value of a region of interest centered on the maximum value from each film and measuring 5×5 mm was used to create the calibration curve. The shape of the acquired curve is consistent with previous studies with radiochromic film and the Intrabeam source.[4]

2.E. Energy response of radiochromic film

EBT2 radiochromic film has previously been shown to have a small energy dependence in the effective energy range relevant to TARGIT.[4] RTQA2 film has a different composition than EBT2 film and so the energy response was investigated. Using the same method described for OSLDs, films were irradiated to doses of 15, 20, and 25 Gy with the 3 and 5 cm applicators at a distance of 0.15 cm to correspond to tumor cavity readings. Likewise films were also irradiated to doses of 1, 3, and 5 Gy for the 3 and 5 cm applicator at distances of 1 and 2 cm to correspond to typical distances between the applicators and the skin. Again at least 24 h was allowed in between irradiation and scanning of the radiochromic film to allow time for stabilization. The films were scanned using the technique described previously and the calibration curve was applied. A region of interest was set to 5×5 mm and the average doses recorded for the center of each film.

2.F. Absorption in RTQA2 film

The same method used for OSLDs was repeated for RTQA2 film to measure the radiative absorption. The film was secured to the brown housing in the water phantom and a 34013 PTW ionization chamber was placed in a holder in the brown housing with the film completely covering the active volume of the chamber at a point 0.15 cm from the effective point of measurement of the ionization chamber. Readings were taken with the bare needle tip of the Intrabeam placed at distances of 0.5, 1.0, 1.5, and 2.0 cm from the effective point of measurement of the ionization chamber. The measurements were repeated without the film and the resulting absorption was calculated.

2.G. *In vivo* measurements

Both types of dosimeters used in this study were placed on the skin edge at positions superior and inferior to the applicator. Figure 3 shows a typical setup. An OSLD nanoDot can be seen inferior to the applicator. Because the skin has been retracted from the applicator to reduce dose, the skin dosimeters were typically 1–2 cm from the edge of the applicator and at least 1 cm from the x-ray source, depending on the depth of the tumor cavity. The skin distance from applicator was confirmed to be at least 1 cm in each case using ultrasound. The 1 cm skin eversion is recommended because a case of necrosis was reported in the first trials of the Intrabeam and in consideration of the potential doses received inside that distance being greater than 6 Gy, the threshold for skin damage after a single exposure from x-ray.[4,14,15]

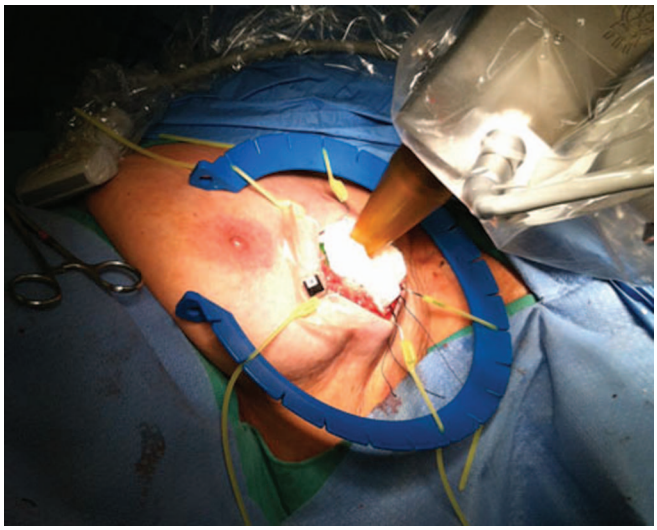

FIG. 3. Dosimeter placement during treatment.

TABLE I. Comparison of doses delivered from the 3 and 5 cm applicators to OSLDs. Uncertainties are calculated as one standard deviation of measurements.

Distance from applicator surface (cm)	Dose delivered (Gy)	3 cm applicator Dose OSLD (Gy)	5 cm applicator Dose OSLD (Gy)	Combined results Dose OSLD (Gy)
0.15	15.0 ± 0.1	15.4 ± 0.9	15.4 ± 0.1	15.4 ± 0.5
0.15	20.0 ± 0.1	18.7 ± 0.4	20.2 ± 0.2	19.5 ± 0.9
0.15	25.0 ± 0.2	23.4 ± 1.4	24.0 ± 0.1	23.7 ± 0.9
1	1.0 ± 0.0	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1
1	3.0 ± 0.0	2.6 ± 0.1	2.7 ± 0.2	2.7 ± 0.1
1	5.0 ± 0.1	4.4 ± 0.0	4.7 ± 0.2	4.6 ± 0.2
2	1.0 ± 0.0	1.0 ± 0.1	1.0 ± 0.0	1.0 ± 0.1
2	3.0 ± 0.0	2.6 ± 0.1	2.5 ± 0.1	2.6 ± 0.1
2	5.0 ± 0.1	4.8 ± 0.7	4.2 ± 0.2	4.5 ± 0.5

The cavity dosimeter was placed by the breast surgeon at the bottom of the tumor cavity before the applicator was inserted and stitched in place. No special measures were taken to ensure that the dosimeter remained in place during treatment and it is probable that some shifted position after the purse-string stitch was tightened to conform the breast tissue to the applicator. It is also possible that a gap existed between the applicator and some of the dosimeters.

Radiochromic films were cut to approximately 2.54 × 2.54 cm, placed in a plastic bag, and sealed between two pieces of Tegaderm before placing them on the patient. After treatment delivery the films were recovered, removed from the plastic bag, and scanned for analysis. At least 24 h were allowed between recovery of the films and scanning to allow time for the films to stabilize. During analysis the calibration curve was applied to each film and a region of interest was selected that was approximately 1 mm from the film edge in all directions. The cavity films were completely exposed and average, maximum, and minimum doses were recorded. Films used to record skin dose exhibited a rapid dose falloff as a function of distance from the applicator with portions of the films receiving very low doses (<0.1 cGy). It was decided that the maximum film reading was the value of interest for skin dose measurements for reporting purposes.

A similar procedure was used for placement and sterile packaging of the OSLD dosimeters. The OSLDs were recovered and read with the Inlight MicroStar dosimetry system. The net counts were recorded and all three calibration factors were applied to obtain dose readings.

3. RESULTS

3.A. Energy response of OSLDs

The OSLD response to delivered doses from the 3 and 5 cm applicators are shown in Table I. Measurements made at a distance of 0.15 cm resulted in percentage differences that ranged from −6.6% to 2.8%. Among the measurements made at 1 and 2 cm distances, the percentage differences ranged from −16.5% to 3%. There is a trend of increasing percentage difference with distance from the applicator surface for an individual applicator, but there was no discernible trend in measurements made at the same distance with the 3 and 5 cm applicators.

3.B. Absorption of OSLDs and RTQA2 film

The results of the measurements for the radiative absorption by the OSLDs and film are summarized in Table II. The OSLD absorption is negative indicating that the OSLD absorbs less radiation than the water it displaces. This result was further investigated by disassembling an OSLD and measuring the absorption through the component pieces. The absorption through the plastic case is negative but absorption through the Al_3O_3 infused disk inside the nanoDot is positive indicating the radiative absorption is higher than water.

Previous works have measured absorption of 3% in EBT2 radiochromic film with the Intrabeam accelerator at a distance of 2.3 cm from the film in air.[4] The absorption of RTQA2

TABLE II. Percent absorption measured at set distances between the Intrabeam needle tip and the effective point of measurement of the ionization chamber. Uncertainties are calculated as one standard deviation of measurements.

	0.5 cm	1.0 cm	1.5 cm	2.0 cm
OSLD	− 20.5 ± 0.3	− 9.1 ± 0.2	− 5.8 ± 0	− 4.1 ± 0.5
OSLD Al_3O_3 disk		5.9 ± 0.2		
Half of OSLD plastic case		− 11.3 ± 0.1		
RTQA film	8.5 ± 0.2	4.8 ± 0.2	3.2 ± 0.2	2.6 ± 0

TABLE III. Comparison of doses delivered from the 3 and 5 cm applicators to film. Uncertainties are calculated as one standard deviation of measurements.

Distance from applicator surface (cm)	Dose delivered (Gy)	3 cm applicator Dose film (Gy)	5 cm applicator Dose film (Gy)	Combined results Dose film (Gy)
0.15	15.0 ± 0.1	14.6 ± 0.7	15.9 ± 0.1	15.3 ± 0.8
0.15	20.0 ± 0.1	19.6 ± 0.1	19.1 ± 0.1	19.3 ± 0.3
0.15	25.0 ± 0.2	23.3 ± 0.1	23.5 ± 0.1	23.4 ± 0.1
1	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0
1	3.0 ± 0.0	2.9 ± 0.0	3.2 ± 0.0	3.1 ± 0.1
1	5.0 ± 0.1	5.4 ± 0.0	5.3 ± 0.0	5.3 ± 0.1
2	1.0 ± 0.0	1.1 ± 0.0	1.0 ± 0.0	1.1 ± 0.0
2	3.0 ± 0.0	3.1 ± 0.0	3.0 ± 0.0	3.1 ± 0.1
2	5.0 ± 0.1	5.4 ± 0.1	5.4 ± 0.1	5.4 ± 0.1

film varied with the distance from the applicator, ranging from 8.5% at 5 mm distance to 2.6% at 20 mm distance. Given the similar composition of EBT2 and RTQA2 film, it is reasonable that the absorption values are consistent.

3.C. Energy response of RTQA2 film

Table III lists the results of measurements taken to characterize the energy response of RTQA2 film. The results show good agreement between measured and delivered doses close to the surface of the applicator. The percentage differences for measurements taken at a distance of 0.15 cm ranged from −6.8% to 6.2%. Previously reported values for EBT films taken for the measurement of percentage depth doses agreed with ion chamber measurements within 6.9%.[8]

The measurements taken at distances of 1.0 and 2.0 cm vary in percentage difference from −1.8% to 8.0%. Among all water phantom film measurements there was an average percentage difference of 0.6% ± 5.2. There is no discernible trend between percentage difference and applicator size or distance from applicator surface.

3.D. *In vivo* measurements

The results of *in vivo* measurements for radiochromic film and OSLD measurements are summarized in Tables IV–VI. All treatments were delivered with a dose of 20 Gy prescribed to the surface of the applicator. Film measurements were taken on 20 patients and OSLD measurements were taken on 10 patients.

The radiochromic film readings for the cavity resulted in an average of 18.2 ± 3.3 Gy. The skin doses for superior and inferior locations were 2.1 ± 0.7 and 2.1 ± 0.8 Gy, respectively. Average values of individual cavity film measurements ranged from 7.8 to 22.5 Gy and the average difference between planned dose and film measurement was −10.1%. Table VI displays the average difference based on dosimeter and applicator size and also reports the number of times each applicator was used. Superior and inferior skin maximum film value measurements ranged from 0.7 to 3.5 Gy.

OSLD measurements resulted in an average cavity dose reading of 15.9 ± 3.9 Gy. The average difference between measured and planned dose on the applicator surface was −20.6%. Skin dose measurements covered a range of values from 0.5 to 3.9 Gy.

4. DISCUSSION

4.A. Energy response and uncertainty of OSLDs

Previous studies have demonstrated the energy dependence of OSLDs at diagnostic energies.[11] In this study we tested the stability of OSLD readings taken over the energy range of TARGIT. These experiments tested both the response of the OSLD dosimeters with the change in effective energy due to applicator over the range of applicator sizes and the change in effective energy due to increased distance.

There was no consistent variation in readings taken with OSLDs due to the size of the applicator either in readings taken near the surface of the applicator or at a distance. Differences between expected and measured values at a depth of 0.15 cm ranged from −6.6% to 2.8%. The measurements

TABLE IV. Results of *in vivo* dosimetry with radiochromic films in intraoperative breast radiotherapy for 20 patients.

Site of measurement	Cavity Minimum (Gy)	Cavity Maximum (Gy)	Cavity Average (Gy)	Superior Maximum (Gy)	Inferior Maximum (Gy)
Average	7.2	22.1	18.2	2.1	2.1
Standard deviation	3.5	2.6	3.3	0.7	0.8

TABLE V. Results of *in vivo* dosimetry with OSLD dosimeters for 10 patients.

Site of measurement	Cavity Reading (Gy)	Superior Reading (Gy)	Inferior Reading (Gy)
Average	15.9	1.2	1.5
Standard deviation	3.9	0.6	1.0

TABLE VI. Average percentage difference between measured and planned dose in the cavity with OSLDs and radiochromic film and the number of times each applicator was used.

Applicator (number of times used)	3 cm (1)	3.5 (0)	4 (3)	4.5 (3)	5 (3)
OSLD	−1.0		−21.8	−30.3	−13.6
Applicator (number of times used)	3 cm (3)	3.5 (4)	4 (8)	4.5 (5)	5 (0)
RTQA2	6.3	−7.3	−11.0	−16.6	

taken at 1.0 and 2.0 cm exhibited much higher percentage differences with a maximum value of −16.5%. Previous investigators using EBT radiochromic films reported agreement of 6.9% with a PTW ionization chamber of type 23342, when calibrating the films for measurement of percent depth doses of the Intrabeam with different applicators.[8] Using our calibration technique OSLD readings at the surface of the applicator can be conservatively assigned an uncertainty of ±7% and readings taken up to 2.0 cm are reliable within approximately ±17%. The surface reading uncertainty reported here is the same as the total quoted uncertainty of 17% reported for TLD measurement in IORT.[14] While the uncertainty for readings taken at increased distances from the applicator surface is high, these measurements correlate to readings taken on the skin surface where the expected dose is typically less than 5 Gy. A 17% uncertainty may be considered acceptable at such doses considering the absolute dose error at a reading of 5 Gy is less than 1 Gy.

4.B. Absorption of OSLDs and film

It was important to quantify the radiation being absorbed by the dosimeters used in the tumor cavity to assure that they were not negatively impacting clinical outcomes. Experimental results indicate that the absorption in OSLDs can vary from −20.5% to −4.1% depending on the distance from source. This surprising result led to further investigation of the radiative absorption through the components of the OSLD. The plastic that comprises the OSLD case absorbs less radiation than the water it displaces. The case also creates an air pocket that contributes to the effect. Though the plastic disk inside the OSLD absorbs 5.9% of the radiation, the influence of that disk on overall absorption through the OSLD is offset by the plastic case. This certainly does not indicate that tissue obscured by the OSLD is receiving an enhanced dose, but demonstrates that if 2 mm of tissue was replaced by the OSLD then the underlying tissue would receive an increased dose. This is not the case, however, as the tissue is not replaced but displaced by the OSLD. For this reason a conservative absorption value of 5.9% was adopted for OSLDs that reflects the maximum absorption measured through any component of the dosimeter.

Absorption by the film varied from 2.6% to 8.5%. Treatments in this study were given with a prescription of 20 Gy to the surface of the applicator. Adopting the 8.5% absorption, as a worst case scenario approach and adjusting the delivered dose based on the measured absorption, the tissue under the film receives 18.3 Gy, under ideal conditions of perfect tissue conformance and Intrabeam performance. Other clinicians have adopted a method of prescribing 5 Gy at a depth of 1 cm.[4] Using this method the dose at the surface of the applicator is 17.1, 19.8, 17.5, 15.9, and 14.7 Gy for the 3, 3.5, 4, 4.5, and 5 cm applicators. It was concluded that absorption of 8.5% is acceptable when weighed against the value of *in vivo* measurements and compared to other methods of administering TARGIT. A similar argument supports the use of OSLDs with 5.9% absorption.

4.C. Energy response and uncertainty of RTQA2 film

There was a concern that RTQA2 film could not be used for TARGIT dosimetry because it has a white polyester backing making it impossible to use a transmission type scan and because it has a dynamic range listed by the manufacturer of 0.02 to 8 Gy, which does not cover the entire range of interest for TARGIT *in vivo* dosimetry. The results of this work demonstrate that RTQA2 film produces satisfactory dosimetric results for the range of doses delivered in TARGIT radiotherapy. There was no discernible trend in film response with the change in effective energy. The maximum percentage difference measured between RTQA2 film readings and delivered dose was 8% and an average percentage difference was 0.6% ± 5.2%. It is reasonable to assume a worst case scenario uncertainty of ±8% for RTQA2 film readings. This uncertainty agrees with reported uncertainty for EBT film of 6.9%.[8] A future research study is recommended to fully evaluate the dosimetric characteristics, including dynamic range, of RTQA2 film when used with diagnostic energies and a reflective flatbed scanner like the one used in this study.

4.D. *In vivo* measurements

In vivo dosimetry in many forms has been implemented in radiotherapy to assure safe and accurate dose delivery. Such measurements check the dose delivered to the patient rather than the individual components prior to treatment.[16] Dosimetric measurements taken in the first few fractions of EBRT can confirm that the planned dose is being delivered within an acceptable tolerance and will alert the clinician to potential problems early in the course of treatment. Though the TARGIT approach is delivered in one fraction, there is still merit in performing *in vivo* dosimetry. It is reasonable to establish a metric for confirming that a therapeutic dose of radiation is delivered to each patient receiving intraoperative breast radiation. Radionecrosis of the skin was reported in one patient of the pilot study for TARGIT, indicating that

monitoring of skin dose is also warranted for this procedure.[17] Moreover such dosimetric measurements acquired for a population of patients serves as a form of process quality assurance.

OSLDs offer a fast way to perform *in vivo* dosimetry for TARGIT patients. They are small in size, allowing them to be placed in the tumor cavity and on the skin. The energy response has been shown to extend into the diagnostic range of energies that are being used in TARGIT.[18] Additionally the process of reading OSLDs can be completed in a few minutes, meaning results are readily available to assess the potential impact to the patient. This work has demonstrated that OSLD response is sensitive to the beam quality. This effect is apparent in the increasing uncertainty with distance from the applicator. The nonlinear calibration accounts for the supralinear response to doses above 2 Gy and produces results that are comparable to previously published values. Cavity measurements were reported with average percentage differences between delivered and measured doses of 1.0%, −21.8%, −30.3%, and −13.6% for the 3, 4, 4.5, and 5.0 cm applicators respectively and an overall average difference of −20.6%. Avanzo *et al*. reported applicator surface dose average percentage differences of −27.6%, −19.9%, −11.9%, and −10.4% for the 3.5, 4, 4.5, and 5.0 cm applicators, with an average difference of −19.0%.[4]

Skin dose measurements are influenced by many factors that vary from case to case such as distance of the skin to the applicator surface, applicator selected, etc. OSLDs produced readings that ranged from 0.5 to 3.9 Gy. The range of these results is comparable to previous studies which have reported 2.2 ± 1.0, 2.9 ± 1.5, and 2.9 ± 1.6 Gy for skin dose measurements taken 1–2 cm from the applicator using both EBT2 radiochromic film and TLDs.[4,5,14]

RTQA2 film has been demonstrated in this work to produce *in vivo* dosimetry measurements that are consistent with EBT2 radiochromic film, TLDs, and OSLDs. The tumor cavity measurements for radiochromic film produced average differences between delivered and measured doses of 6.3%, −7.3%, −11%, and −16.6% for the 3, 3.5, 4, 4.5, and 5 cm applicators, with an average difference of −10.1% for all applicators. This average error is lower than that found by a previous work.[4] The range of skin dose measurements was 0.7 to 3.5 Gy, which is comparable to the previously cited values. Radiochromic film offers several advantages in dosimetric readings for TARGIT. The film can be cut into any size and shape allowing it to be optimized for placement on the patient and in the tumor cavity. TARGIT requires a small dosimeter, such as film, due to the steep dose gradients. Radiochromic film also does not require processing like conventional silver halide film; although a potential drawback is that it must be allowed sufficient time to stabilize before it can be evaluated. The 24 h stabilization period used in taking measurements for this study was not found to be prohibitive.

A two-tailed statistical significance test was performed to determine the differences between OSLDs and RTQA2 film data for the tumor cavity. This analysis resulted in a value of $p = 0.1$. Adopting a 0.05 level of confidence, the results show no statistical difference between the OSLD and film data. A similar test done for skin dose measurements resulted in $p < 0.01$. This does indicate that for measurements taken on the skin there is a statistically significant difference between OSLD and film readings.

As has been stated, TARGIT necessitates that any *in vivo* measurements be performed with a small dosimeter due to the steep dose gradient involved. For the same reason the dosimeter must be carefully positioned. Previous work involving quality assurance of the Intrabeam system noted that the largest source of error associated with ion chamber and film is the positioning of the dosimeter.[19] The positioning of the cavity dosimeter for the *in vivo* measurements done in this work was not carefully monitored. It is thought that the occasional very low dose reading seen with OSLDs and film in the cavity are due primarily to poor dosimeter positioning in the patient and not due to a delivered dose that is lower than the prescription dose. This assumption is supported by the stability of the readings over dose, for OSLDs and radiochromic film taken in the water phantom.

The dose falloff with depth in tissue is steep as a result of the low energy. The percentage depth dose at 1 mm averaged over all applicators is 86%. Assuming an OSLD was 1 mm from the applicator and that the tumor cavity was filled with fluid the readings could range from 16.2 to 18.4 Gy given a ±7% uncertainty and a prescription of 20 Gy to the surface of the applicator. At 2 mm the percentage depth dose averaged over all applicators is 76%. Using the same uncertainty this would result in OSLD readings that range from 14.1 to 16.2 Gy. There were only two readings lower than 15 Gy in the data so it is likely most OSLDs were within 2 mm of the applicator.

The same argument can be applied to film dosimetry. Using a ±8% uncertainty at a distance of 1 mm from the applicator for a prescription of 20 Gy the RTQA2 film readings could range from 15.9 to 18.6 Gy. At a 2 mm distance the range is 14 to 16.4 Gy. Assuming the maximum distance from applicator to either type of dosimeter in the tumor cavity is 2 mm, the estimated uncertainty of OSLDs and RTQA2 film for *in vivo* dosimetry is in the range of 30%–40%. These calculations emphasize the importance of accurate dosimeter placement during treatment. Previous studies have used ultrasound to ensure that the dosimeter is in contact with the surface of the applicator, and that method is being adopted by the authors for future work.[4]

There is an argument that can be made for not confirming dosimeter placement. Now that the uncertainty under ideal conditions has been established, an unusually low reading could point toward poor tissue conformance during treatment which may indicate that further radiotherapy is warranted.

Even using ultrasound guidance to ensure accurate dosimeter placement Avanzo *et al*. reported an average difference between planned dose on the applicator surface and measured dose of −19.0% which indicates another factor contributing to the error in surface dose readings.[4] As other researchers have noted, the values of the surface doses reported by the Intrabeam treatment planning system are derived by extrapolation of manufacturer measurements at

shallower depths.[19] The uncertainty of tumor cavity dosimetric measurements may also reflect the uncertainty in reported values at the applicator surface.

5. CONCLUSIONS

The measurements taken during treatment provide a quality assurance check for the Intrabeam intraoperative radiotherapy modality and a method by which to measure skin dose. In this study it was demonstrated that RTQA2 radiochromic film is superior to optically stimulated luminescence dosimeters for *in vivo* dosimetry in TARGIT, due to the lower uncertainty of readings taken at a distance from the applicator and a clearer understanding of films impact on the dose to underlying tissue.

A nonlinear calibration curve was established using the Intrabeam for OSLDs and the characteristics of the OSLDs were tested. The nonlinear calibration produced *in vivo* results that agreed with previously published data. The influence of the energy dependence of OSLDs was not observable between applicators but does become apparent at distances of 1–2 cm from the surface of the applicator. Radiative absorption by the Al_3O_3 infused plastic disk inside the OSLD was measured as 5.9% which was determined not to be prohibitive.

A nonlinear calibration curve was also established for RTQA2 radiochomic film. RTQA2 radiochromic film readings for cavity measurements were found to have better average agreement with the expected applicator surface dose than previously published data taken with EBT2 radiochromic film. Skin dose measurements taken with RTQA2 film were found to be consistent with measurements taken with both EBT2 radiochromic film and TLD. The energy dependence of RTQA2 film was found to be negligible and water phantom measurements found that over the energy range and doses used in TARGIT RTQA2 films have an estimated uncertainty of $\pm 8\%$. A maximum radiative absorption through the film was measured to be 8.5%, but this was not considered prohibitive when compared to applicator surface doses from other treatment paradigms used in TARGIT.

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[1]J. S. Vaidya, D. J. Joseph, J. S. Tobias, M. Bulsara, F. Wenz, C. Saunders, M. Alvarado, H. L. Flyger, S. Massarut, W. Eiermann, M. Keshtgar, J. Dewar, U. Kraus-Tiefenbacher, M. Sütterlin, L. Esserman, H. M. R. Holtveg, M. Roncadin, S. Pigorsch, M. Metaxas, M. Falzon, A. Matthews, T. Corica, N. R. Williams, and M. Baum, "Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): An international, prospective, randomised, non-inferiority phase 3 trial," Lancet **376**, 91–102 (2010).

[2]M. Essers and B. Mijnheer, "In vivo dosimetry during external photon beam radiotherapy," Int. J. Radiat. Oncol., Biol., Phys. **43**, 245–259 (1999).

[3]P. D. Higgins, P. Alaei, B. J. Gerbi, and K. E. Dusenbery, "In vivo diode dosimetry for routine quality assurance in IMRT," Med. Phys. **30**, 3118–3123 (2003).

[4]M. Avanzo, A. Rink, A. Dassie, S. Massarut, M. Roncadin, E. Borsatti, and E. Capra, "In vivo dosimetry with radiochromic films in low-voltage intraoperative radiotherapy of the breast," Med. Phys. **39**, 2359–2368 (2012).

[5]D. J. Eaton, B. Best, C. Brew-Graves, S. Duck, T. Ghaus, R. Gonzalez, K. Pigott, C. Reynolds, N. R. Williams, and M. R. Keshtgar, "In vivo dosimetry for single-fraction targeted intraoperative radiotherapy (TARGIT) for breast cancer," Int. J. Radiat. Oncol., Biol., Phys. **82**, e819–e824 (2012).

[6]C. J. Yahnke, "Calibrating the microStar," InLight TM Landuaer, Inc. 2010 (internal report).

[7]M. Dinsmore, K. J. Harte, A. P. Sliski, D. O. Smith, P. M. Nomikos, M. J. Dalterio, A. J. Boom, W. F. Leonard, P. E. Oettinger, and J. C. Yanch, "A new miniature x-ray source for interstitial radiosurgery: Device description," Med. Phys. **23**, 45–52 (1996).

[8]D. J. Eaton and S. Duck, "Dosimetry measurements with an intra-operative x-ray device," Phys. Med. Biol. **55**, N359–N369 (2010).

[9]C. S. Reft, "The energy dependence and dose response of a commercial optically stimulated luminescent detector for kilovoltage photon, megavoltage photon, and electron, proton, and carbon beams," Med. Phys. **36**, 1690–1699 (2009).

[10]Landauer, *Landauer microStar User Manual* (Landauer Inc., Glenwood, IL, 2008).

[11]R. M. Al-Senan and M. R. Hatab, "Characteristics of an OSLD in the diagnostic energy range," Med. Phys. **38**, 4396–4405 (2011).

[12]Zeiss, *Intrabeam Water Phantom User Manual* (Carl Zeiss Meditec AG, Jena, Germany, 2011).

[13]P. A. Jursinic, "Changes in optically stimulated luminescent dosimeter (OSLD) dosimetric characteristics with accumulated dose," Med. Phys. **37**, 132–140 (2010).

[14]P. Fogg, K. R. Das, T. Kron, C. Fox, B. Chua, and J. Hagekyriakou, "Thermoluminescence dosimetry for skin dose assessment during intraoperative radiotherapy for early breast cancer," Australas. Phys. Eng. Sci. Med. **33**, 211–214 (2010).

[15]J. Geleijns and J. Wondergem, "X-ray imaging and the skin: Radiation biology, patient dosimetry and observed effects," Radiat. Prot. Dosim. **114**, 121–125 (2005).

[16]E. Yorke, R. Alecu, L. Ding, D. Fontenla, A. Kalend, D. Kaurin, M. E. Masterson-McGary, G. Marinello, T. Matzen, A. Saini, J. Shi, W. Simon, T. C. Zhu, and X. R. Zhu, "Diode *in vivo* dosimetry for patients receiving external beam radiation therapy," *Report of Task Group 62 of the Radiation Therapy Committee* (Medical Physics, Madison, WI, 2005).

[17]J. S. Vaidya, M. Baum, J. S. Tobias, D. P. D'Souza, S. V. Naidu, S. Morgan, K. J. Harte, A. P. Sliski, and E. Thomson, "Targeted intraoperative radiotherapy (Targit): An innovative method of treatment for early breast cancer," Ann. Oncol. **12**, 1075–1080 (2001).

[18]P. A. Jursinic, "Characterization of optically stimulated luminescent dosimeters, OSLDs, for clinical dosimetric measurements," Med. Phys. **34**, 4594–4604 (2007).

[19]D. J. Eaton, "Quality assurance and independent dosimetry for an intraoperative x-ray device," Med. Phys. **39**, 6908–6920 (2012).