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FULL ARTICLE

Light-guided lumpectomy: first clinical experience

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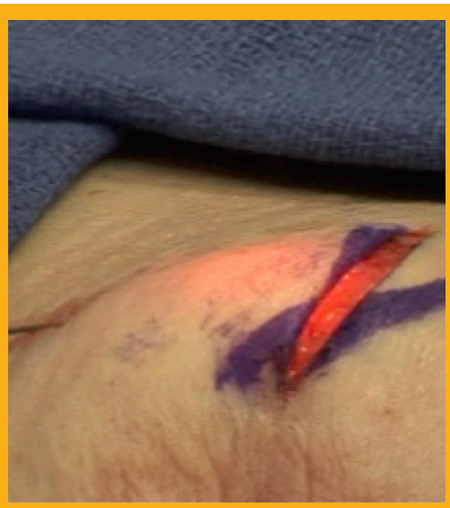
Despite numerous advances, lumpectomy remains a challenging procedure. We report on the early use of light-guided lumpectomy. Eight patients with non-palpable breast cancer undergoing lumpectomy for biopsy-proven and radiographically identifiable cancer were enrolled in the study. An optical wire was designed that incorporated a standard hook-wire with an optical fiber. The optical wire was placed in the same manner as a standard hook-wire. During light-guided lumpectomy, an eye-safe laser illuminated the optical wire and created a sphere of light surrounding the cancer. The light was visible at the beginning of each surgery and facilitated approaching the cancer without using the wire. Dissection around the sphere of light kept the wire tip within the surgical specimen. Three of eight initial surgical specimens had focally positive margins. Additional cavity shaves were performed during five lumpectomies and resulted in negative margins in seven of eight patients. Light-guided lumpectomy is a minor change to breast conserving surgery that can be easily incorporated into clinical practice. Further investigation into the clinical benefit of light-guided lumpectomy is warranted.



Red light located within a breast lesion is emitted through the skin during breast conserving surgery.

1. Introduction

Surgical management of breast cancer has been evolving over the last two decades. It is estimated that three out of four breast cancer patients are eligible for breast conserving therapy [1] and the occurrence of breast conserving surgery has increased in the last decade [1–3]. In 2006, 347,000 lumpectomies and 70,000 mastectomies were performed in the U.S. [4, 5].

It has been demonstrated that lumpectomies with negative margins followed by breast irradiation have equivalent 12 year ipsilateral recurrence rates as

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mastectomies for tumors less than 4 cm in diameter with negative or positive axillary lymph nodes [6]. Upon 20 year follow up, disease-free and overall survival following lumpectomy with negative margins and X-ray irradiation were not statistically different from those treated with mastectomy [7]. However, margin negative lumpectomy remains challenging [8, 9]. Margin status is critical to success of the treatment with most studies reporting 20–40% positive margins following lumpectomy [10, 11]. If a margin is positive following lumpectomy, the patient usually undergoes a second surgery to clear the margins. Positive margins not only increase risk of ipsilateral breast tumor recurrence [10, 12] but also prolong the course of treatment, create additional cost and potentially affect the cosmetic result. One suggested explanation for the high positive margin rate is lack of tumor visibility during surgery [8].

The feasibility of using low-power eye-safe light as a beacon in breast tissue, has been demonstrated [13]. Figure 1 shows the light distribution at the surface of excised human breast tissue when the light source was 20 and 50 mm deep in both a lit and dark room. Similar observations have been reported where red light could be seen through several centimeters of breast tissue [14]. We were initially concerned that the diffuse glowball (30–60 mm in diameter) would make it difficult to determine the center. However, gentle pressure on the breast tissue clearly indicated the direction to the source by reducing the distance between the source and the surface. The path between the source and the location of the pressure appeared brighter than the surrounding areas of tissue.

A visible glowball of light centered within a tumor may be able to assist in both locating and resecting it. This is a report on the first eight uses of light-guided lumpectomy. Light was used as a simple method for isolating the tissue volume surrounding a breast tumor.

2. Materials and methods

Eight patients provided informed witnessed consent and were enrolled in an institutional review board approved study. Patients with non-palpable breast cancer (<2 cm diameter) undergoing lumpectomy for biopsy-proven radiographically identifiable disease were eligible. We did not exclude patients based on type of breast cancer, neoadjuvant chemotherapy, or age. Patients were recruited from the patient population of one surgeon at one institution. Patients were between 41 and 68 years old undergoing lumpectomy to remove ductal carcinoma *in situ* (3 patients) or invasive ductal carcinoma (5 patients), Table 1. One patient was treated with neoadjuvant chemotherapy prior to lumpectomy. Five patients underwent sentinel lymph node biopsy at the time of lumpectomy.

2.1. Optical wire

Optical wires [13] instead of hook-wires [15] were used to localize tumors. Each optical wire was composed of a biocompatible polyimide sheathed 200 μm optical fiber (Optran WF 200/220 P, CeramOptec, East Longmeadow, MA) attached to a 20 cm long Kopans breast lesion localization wire (DKBL-20-9.0, Cook Medical Inc., Bloomington, IN) using medical-grade ultraviolet-curing acrylic (Loctite 392, Henkel Corporation, Bay Point, CA). The outer diameter of the optical wire was 457 μm. The total length of the optical fiber was 3 meters. The light emitting end of the optical fiber was offset 2–3 mm from the tip of the Kopans wire to allow the entire optical wire to pass though an 18 gauge needle (Figure 2).

2.2 Wire localization

The center of the tumor was targeted during localization. An 18 gauge needle was placed in the breast using either mammography or ultrasound guidance. The optical wire was advanced through the needle until the spring hook was aligned with the tip of the needle. Imaging confirmation of placement within the tumor was achieved and the needle was removed allowing the hook to deploy. Orthogonal mammograms were taken to verify the location of the wire relative to the tumor and to the previously placed

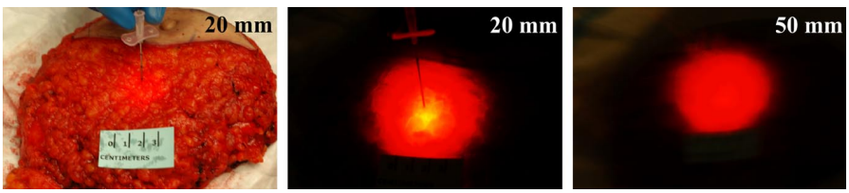

Figure 1 (online color at: www.biophotonics-journal.org) Red light emission from excised human breast tissue with the source 20 and 50 mm deep as labeled, (*left* room lights on, *middle & right* room lights off).

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Table 1 Radiographic and Operative metrics for enrolled patients. IDC: invasive ductal carcinoma, DCIS: ductal carcinoma *in situ*. Breast Comp. is the BI-RADS breast composition score. Wire-to-clip is the distance between the wire tip and the biopsy clip in both the cranio-caudal [CC] and latero-medial [LM] projections. The wire depth is the distance from the wire tip to the skin. The light emitted through fiber is the percentage of total laser power used during the approach/resection portion of the lumpectomy.

Patient ID	1	2	3	4	5	6	7	8
Age [years]	67	51	65	41	61	68	53	59
Initial Diagnosis	IDC	IDC	DCIS	IDC	IDC	IDC	DCIS	DCIS
Breast Comp.	3	3	4	4	2	2	2	1
Wire-to-Clip [cm]								
CC	0.5	0.1	0.2	0.1	0.4	0.4	0.6	0.5
LM	0.4	0.1	0.2	0.8	0.1	0.1	0.2	0.2
Wire Depth [cm]	5	5	4	6	5	5	3	6
Light seen through skin	No	Yes	No	Yes	No	Yes	Yes	Yes
Light emitted through fiber [%]	100/100	100/100	100/100	100/30	100/30	100/100	100/30	100/70

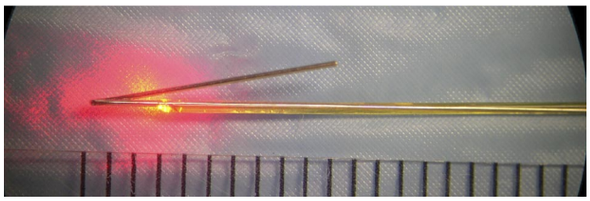

Figure 2 (online color at: www.biophotonics-journal.org) A light emitting optical wire composed of a 200 μm optical fiber adhered to the length of a standard hook-wire. The light emitting tip of the optical fiber is offset 2–3 mm from the distal, hooked tip of the wire. The ruler is in units of millimeters.

biopsy clip, Figure 3. Finally, the external portion of the optical wire was secured to the breast with gauze and tape.

Breast density was recorded based on the Breast Imaging-Reporting and Data System (BI-RADS) breast composition score of 1–4. Where 1 indicates almost entirely fat, 2 indicates scattered fibroglandular densities, 3 indicates heterogeneously dense, and 4 indicates extremely dense tissue.

2.3 *Light-guided lumpectomy*

Once in the operating room, patients were placed under anesthesia and the tape holding the optical wire in place was removed. The optical wire was connected to a 633 nm HeNe laser with less than 2 mW of light coupled into the fiber. Because the light emitting end of the fiber was within the breast, exact measurements of light output were not possible. However, each fiber had been previously validated to emit 1–2 mW of light. At this low power, laser goggles were not needed, heating of the tissue

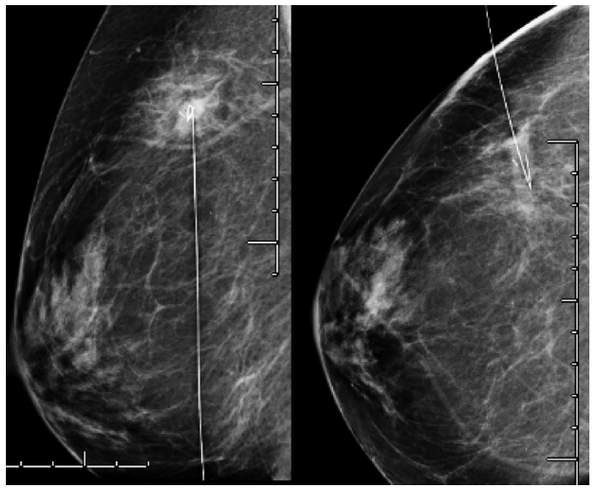

Figure 3 Orthogonal mammograms of one patient after wire localization. The wire was inserted in the lateral to medial direction with its tip in the tumor and approximated to the clip. Rulers are in units of centimeters.

was less than 1 °C, and there was no risk of tissue damage from the light. The light from the laser was focused into the optical fiber using lenses. In lumpectomies 4–8, neutral density filters were used to reduce the intensity of light and consequently the apparent size of the glowball. The filters transmitted either 100, 70, 30, 10 or 1% of the maximum light. Each surgery was started with 100% of the light and the room lights were dimmed in attempt to visualize the red light before making an initial incision. If visible, the brightest area on the skin indicated the shortest approach to the cancer. At the operating surgeon's discretion, the filter was adjusted to change the glowball size around the cancer to approximately 3–4 cm in diameter.

Once the primary specimen had been resected, its six margins were inked by the operating surgeon with six different colors to indicate orientation. The specimen was sent to radiology to confirm that it contained the clip and apparent cancer. Orthogonal radiographs were taken of the specimen with orientation marked on the images. If specimen radiographs or gross appearance of the cavity margins in surgery were suspicious, additional cavity shavings were performed, inked for orientation and sent to pathology.

2.4 Pathology

Each specimen submitted to pathology was placed in formalin, grossly examined, sectioned and stained with hematoxylin and eosin. Cancers were staged according to the American Joint Committee on Cancer Tumor Node Metastasis (TNM) classifications. The specimen size, cancer size, margin status, and pathologic diagnosis were recorded. Margins were considered *positive* for invasive ductal carcinoma if tumor cells were within 1 mm, *close* within 2 mm, and *negative* greater than 2 mm from the margin. Margins were considered *positive* for ductal carcinoma *in situ* if tumor cells were within 2 mm, *close* within 3 mm and *negative* greater than 3 mm from the margin [16].

3. Results

3.1 Wire localization

Each optical wire was placed within a few millimeters of the biopsy clip. In the cranio-caudal projection, the distance from the wire tip to the biopsy clip was 4 ± 2 mm and in the latero-medial projection 3 ± 2 mm. The length of wire within the breast was 50 ± 10 mm. The time of the localization procedure was 21 ± 16 min. The BI-RADS breast composition scores were between 1 & 4, Table 1.

3.2 Light-guided lumpectomy

The glowball was used as a guide in all eight lumpectomies. In 5 patients, with the room lights dimmed, red light was visualized before the first skin incision and provided a clear approach to the targeted tumor. In all patients, the light was readily visualized after skin incision so the light, rather than the wire, dictated the surgical plane. The cancer was approached by sharp dissection towards the brighter light. This was particularly useful for a deep tumor near the chest wall in patient 4. In patients 4–8, the intensity of light was reduced to make the glowball smaller after approach. While keeping the light centered, dissection around the glowball was made. A consistent border around the glowball was obtained by excising along a plane of similar light intensity. After the optical wire and surrounding tissue were removed, the cavity was re-examined. In 5 patients, additional margins were removed due to either suspicious appearance of the cavity or review of specimen radiograph, Table 3. Figure 4 demonstrates the effect of room lighting on visibility of the glowball (top row), as well as how the glowball was used in locating (bottom row, left) and removing the tissue specimen (bottom row, middle & right). The time from first incision to removal of the specimen was 17 ± 6 min and the laser was on for 17 ± 7 min.

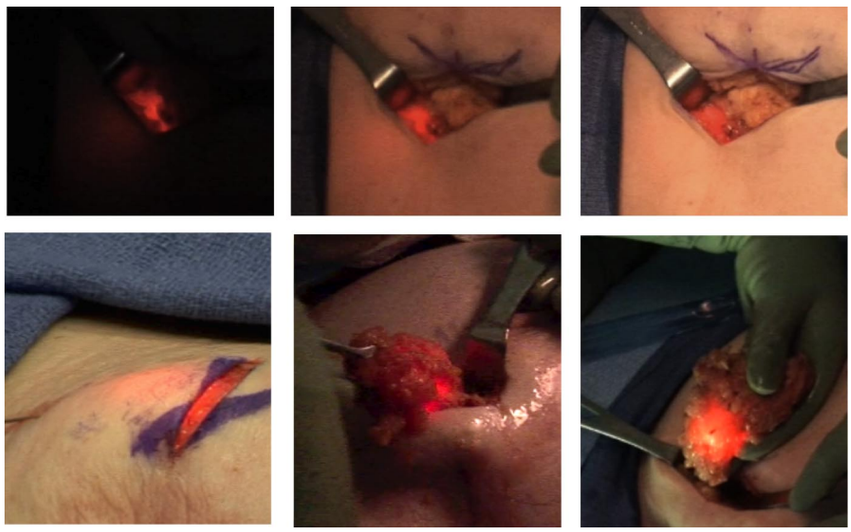

Figure 4 (online color at: www.biophotonics-journal.org) **Top row:** Visibility of a deep (6 cm) glowball near the chest wall as room lighting is increased (*left to right*). **Bottom row:** In practice, (*left*) light guided the surgeon towards the cancer and (*middle & right*) created a visible sphere to remove. The red light can be appreciated well with color images available online.

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3.3 Specimen radiograph

Each specimen was imaged with orientation marked on orthogonal radiographs. The clip was retained in all eight specimens. Figure 5 shows the specimen radiograph for the same patient in Figure 3. The clip and optical wire were centrally located in the specimen.

3.4 Pathology

Although all patients were diagnosed with either IDC or DCIS following core needle biopsy, upon final diagnoses, one patient had only atypical ductal hyperplasia & lobular carcinoma *in situ* remaining in the breast both of which indicate increased risk for breast cancer, Table 2. All four of the patients who underwent sentinel node biopsy were negative for lymph node metastasis. The Nottingham histologic grade for each patient is also shown in Table 2. A high (3) grade classifies poorly differentiated cells that tend to spread and divide more rapidly than moderate (2) and low (1) grades.

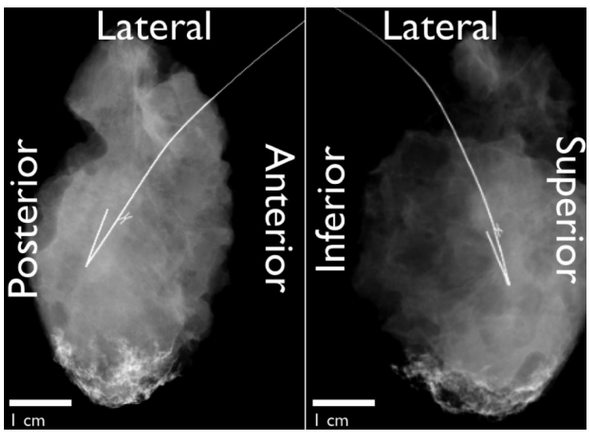

Figure 5 Orthogonal radiographs of the lumpectomy specimen from the breast shown in Figure 3. The optical wire remains approximated to the biopsy clip and centered in the specimen.

Of the primary (light-guided) resections, 3 focally positive margins (1 DCIS, 2 IDC) and 5 negative margins were found. Removal of additional tissue by cavity shaving at the time of initial surgery resulted in negative margins in all but one patient as shown in Table 3. No tumor cells were found in any of the additional margins. In the patient with a positive margin, the primary specimen was excised from the anterior skin to the posterior fascia and additional tissue was excised along the inferior margin at the time of initial surgery. DCIS was found at the anterior and inferior margins, but no skin had been removed at the anterior margin which resulted in re-excision at a later date.

The dimensions of the primary specimens and cancers are shown in Table 4.

4. Discussion

Light-guided lumpectomy is a feasible technique for resecting non-palpable breast tumors that was easily incorporated into standard practice. Placement of the optical wire was identical to a standard hook-

Table 2 Pathologic findings following resection(s). IDC: invasive ductal carcinoma, DCIS: ductal carcinoma *in situ*, ADH: atypical ductal hyperplasia (a risk factor for but not a breast cancer). A high (3) Nottingham histologic grade represents poorly differentiated cells that divide more rapidly and tend to spread when compared to moderate (2) and low (1) grades.

Patient ID	1	2	3	4	5	(1	7	8
Final Diagnosis	IDC & DCIS	IDC & DCIS	ADH & LCIS	IDC	IDC & DCIS	IDC & DCIS	IDC & DCIS	DCIS
Node Status [+/total]	0/3	0/1	0/0	0/1	0/1	0/2	0/0	0/0
IDC grade	1	2		3	3	3	2	
DCIS grade	2	3			3	3	3	1

Table 3 Margin status following resection, shortest margin was measured on the primary lumpectomy specimen. IDC: invasive ductal carcinoma, DCIS: ductal carcinoma *in situ*, *: margin focally involved, A: anterior, P: posterior, M: medial, L: lateral, S: superior, I: inferior.

Patient ID	1	2	3	4	5	6	7	8
Shortest Margin: IDC/DCIS [mm]	0/1	5	NA	3	5	0/>5	>5/0	5
Involved Margin(s)	S*	no	NA	no	no	A*	A* I	no
Cavity Shave(s)	S L	no	no	A M L S I	no	A S	I	A M
Neoplasm in Cavity Shave(s)	no			no		no	no	no

Table 4 Specimen and lesion dimensions shown in centimeters. †: residual disease A: anterior, P: posterior, M: medial, L: lateral, S: superior, I: inferior.

Patient ID	1	2	3	4	5	6	7	8
Specimen Size:								
A–P	3.2	2.5	2.5	2.6	3.8	2.5	3.0	4.5
M–L	6.2	3.5	5.6	7.5	5.0	4.8	7.0	8.0
S–I	4.6	4.5	3.5	5.0	4.0	4.5	4.5	6.5
Cancer Size:								
A–P	1.9	0.7		0.3†	1.7	1.3	1.9	0.5†
M–L	1.7	0.6			1.5	1.1	0.9	
S–I	0.9	0.5			1.1	0.9	0.7	

wire. Lumpectomy was facilitated by illumination of tissue as well as a hook-wire. Dissection towards the bright light provided a direct path to the tumor. Once an incision was made in the skin the red light was visible in all patients. The light was visible at 6 cm below the skin which may prove to be particularly useful for deep cancers or for resecting tumors within large breasts. After approach, the glowball provided a visible sphere to dissect around. Ideally, measurements of the distance from the specimen surface to the wire tip would be available to the operating surgeon and is an active area of investigation [17].

The low power laser was comparable to a laser pointer used for presentations; the surgical staff did not need special eye protection. At 1–2 mW of light, the glowball was not visible through the skin in three cases due to either room lighting, fiber coupling or strong attenuation by the skin. All enrolled patients were fair-skinned Caucasians, therefore it was unlikely skin color affected visibility between patients. Higher scattering in skin than breast tissue was the presumed cause of attenuation. It is possible that the light source will not be visible prior to skin incision in patients with darker skin pigmentation due to increased attenuation of the visible light source. However, we chose a visible light source so an imaging system would not be needed during the procedure.

This technique relies on correct placement of the wire tip and relatively uniform absorption and scattering within the tissue to create a sphere of light. It has been reported that the absorption and scattering of cancerous and normal breast tissue differ. In the review by Leff et al., malignant breast tissue had higher absorption than normal tissue for visible red light by approximately two-fold [18] and could effect glowball sphericity. For example, if the wire tip was placed medial to a 2 cm lesion, the light on the lateral side of the lesion may be attenuated more than on the medial side. However, the position of the tip relative to the lesion is known prior to lumpectomy. In addition, a wavelength range of 630–640 nm was selected where absorption by hemoglobin is low, approximately 0.04 cm^{-1} [18], to minimize visual differences between healthy and diseased tissue.

Light-guided lumpectomy does not identify tissue as cancerous, but allows a spherical volume of tissue to be readily resected. It has not been demonstrated that more spherical specimens result in fewer positive margins. However, more spherical specimens may enable treatment with existing partial breast X-ray irradiation and provide a relatively continuous (non-fractured) surface for pathologic examination. A randomized controlled trial is planned to compare the positive margin rate of light-guided and wire-guided lumpectomies. The two groups will be stratified to include equal numbers of patients with both invasive and *in situ* disease.

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