Excerpta Medica

The American Journal of Surgery

The American Journal of Surgery 184 (2002) 359–363

Scientific paper

Laser therapy for small breast cancers

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Manuscript received May 6, 2002; revised manuscript May 27, 2002

Presented at the Third Annual Meeting of the American Society of Breast Surgeons, Boston, Massachusetts, April 24–28, 2002.

Abstract

Background: Widespread mammography has resulted in the increased detection of breast cancer <1.5 cm. It may be possible to treat these small tumors with in-situ laser ablation. Prior to ablation tumor size is determined by ultrasound and mammogram. Histologic diagnosis and determination of prognostic factors are obtained from image-guided needle core samples. Invasive and in-situ tumors may be percutaneously ablated by a stereotactically guided laser needle and subsequently evaluated by imaging methods and needle biopsy.
Methods: Fifty-four patients (50 invasive, 4 in-situ); 51 mass, 3 microcalcification; mean diameter 12 (5 to 23) mm were treated by a stereotactically guided 805 nm laser beam via a fiber in a 16G needle delivered to the cancer. One to 8 weeks later the coagulated lesions were surgically removed for pathologic evaluation. In 2 additional patients, the laser-treated tumors were not removed but were monitored by mammography, ultrasonography, and needle core biopsy.
Results: None of the patients sustained any adverse effect. The average treatment time was 30 minutes. Pathology analysis revealed a 2.5 to 3.5 hemorrhagic ring surrounding the necrotic tumor. Under steady conditions, in two groups of 14 patients, 93% and 100% of the tumors showed complete destruction, with no residual cancer report. In the 2 unresected cases kept under surveillance for 6 to 24 months, the laser-treated tumors first showed shrinkage, followed by a 2 to 3 cm oil cyst. Fibrosis was demonstrated on needle core biopsies.
Conclusions: Laser energy delivered through a stereotactically guided needle appears to ablate mammographically detected breast cancer. A multicenter clinical trail is planned.

Keywords: Laser; Therapy; Breast cancer

Widespread annual screening mammography has resulted in detection of greater percentage of breast cancers measuring 1 cm in diameter [1]. The diagnosis of malignancy and determination of the prognostic factors are made by image-guided needle biopsy. Currently these tumors are surgically removed together with sentinel/regional lymph nodes and the breast is subsequently treated with radiation. Over the past several years at Rush-Presbyterian-St. Luke's Medical Center, a less invasive and esthetically superior technique has been developed which may enable the physician to treat the cancer within the breast with a stereotactically guided laser needle and without the need for its removal. The treatment is applicable to invasive as well as in-situ tumors detected as masses or clusters of microcalcifications. However, the lesion should be circumscribed and be clearly seen by mammography or ultrasound and measure <1.5 cm in diameter.

We have previously reported our experience with smaller number of patients treated with interstitial laser coagulation [2,3]. In this paper we present our expanded experience in 54 patients who, between 1994 and 2001 were treated with interstitial laser therapy of their breast cancers at Rush Presbyterian St. Luke's Medical Center in Chicago. All these patients subsequently underwent surgical removal of the laser-treated lesions 1 to 8 weeks later to determine the rate of complete ablation. Additionally, we briefly describe 2 patients who were treated outside this protocol and were followed up without excision.

Patients and methods

Women of all socioeconomic and racial background older than 21 years with mammographically detected cir-

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0002-9610/02/$ – see front matter
PII: S0002-9610(02)00942-X

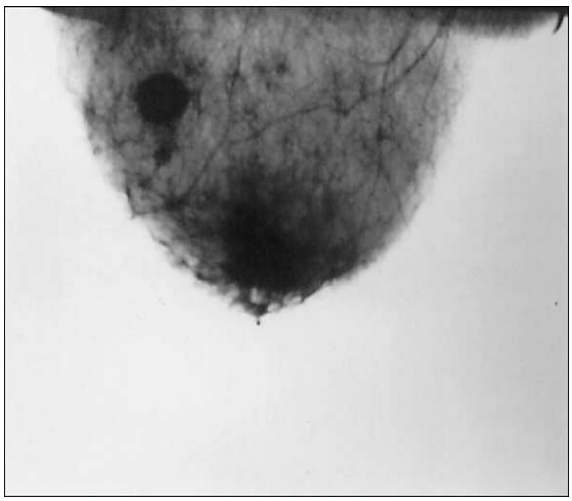

Fig. 1. Mammographic appearance of a circumscribed breast cancer selected for laser therapy.

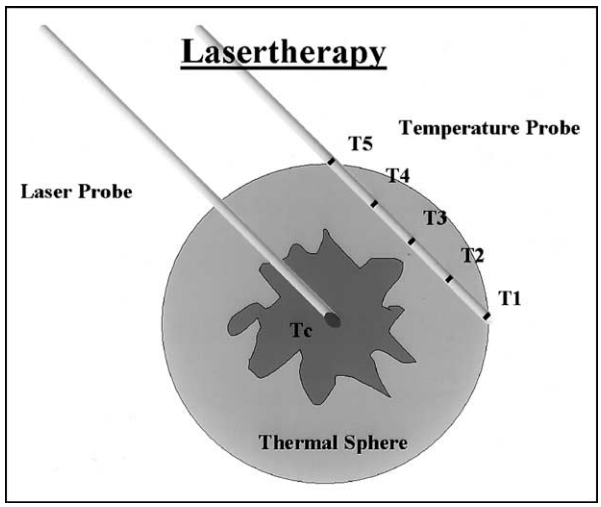

Fig. 2. Schema of laser and a temperature probes in and adjacent to a breast cancer.

cumscribed breast cancers (Fig. 1) were selected and invited to participate in this institutionally approved protocol. The purpose and the nature of the research were discussed in detail with every patient and consent form was obtained. The diagnosis of in-situ or invasive breast cancer was made by image-guided needle biopsy and the prognostic factors were also determined on the needle samples. Each patient was treated with interstitial laser therapy prior to definitive surgical, radiation and if indicated, chemohormonal adjuvant therapy. Two patients opted for laser therapy without surgery and will be briefly discussed.

The technical details of the procedure have been previously described [3]. Briefly, on the day of treatment, the mammographic films were reviewed and the boundaries of the tumor with all its visible extensions plus 0.5 cm of normal appearing tissue were marked on the films. The volume (V) of the tissue sphere for ablation surrounding the tumor was calculated by $V = 4/3\ \pi R3$, R being the radius of the sphere. Our experimental data indicate that for 100% tumor coagulation, 1,400 joules of laser energy per cubic centimeter of the calculated tissue (tumor plus surrounding breast parenchyma) is needed [4,5]. For a typical 1.0 cm tumor plus 0.5 cm ring of surrounding parenchyma, the volume is 4.0 cm^3 and the laser energy for its complete destruction is 5,600 joules. Based on this information a simple table is constructed for tumors measuring up to 1.5 cm in diameters. In practice, the thermal sensors on the needle adjacent to the tumor display the temperatures in real time indicating the adequacy of treatment. When all sensors record 60°C the treatment is completed.

Procedure

Initially, the patient's tumor blood flow is evaluated by contrast enhanced color Doppler ultrasound. She is then positioned on a stereotactic table and the shortest skin-to-tumor route, avoiding any intervening vessels, is chosen. Additional needle core samples are taken from the tumor and archived. Field anesthesia around the tumor is achieved with approximately 50 cc of 0.25% bupivacaine. Four metal markers are inserted around the tumor at positions 3, 6, 9, and 12 o'clock for future reference. The laser needle is inserted into the center of the tumor through a small skin nick and a multisensor thermal needle through a second nick, 1 cm away and parallel with the former, to a predetermined length so that its tip is 1 cm in front of the laser needle (Fig. 2). Stereotactic images are taken to confirm proper positions. The laser needle stylet is replaced with an optic fiber held by a y-connector, the second arm of which is connected to a fluid pump delivering normal saline up to 2.0 cc per minute.

Typically the treatment is commenced by starting the fluid pump at 1.0 cc per minute and the laser power at 5.0 watts. The central temperature from the sensor on the laser needle rises within seconds. The peripheral temperatures begin to rise within a minute when the heat generated by the laser from the center of the tumor reaches them. When all thermal sensors record 60°C, the treatment is stopped. Patient's vital signs are monitored during treatment. Stereotactic images are taken during and at the completion of the procedure to document satisfactory needle alignment. Patients may experience pain during treatment if the initial field anesthesia is inadequate, mandating additional injection of bupivacaine. The skin overlying the tumor may have to be cooled with a coolant spray in cases when the tumor is less than one cm from the skin. At the completion of the treatment, the needles are removed, the breast is decompressed, light dressing is applied, and after 1 hour of observation patient is discharged home with oral analgesics and ice pack on the breast.

All patients underwent wire localization, surgical excision of the tumor, and removal of the regional lymph nodes. The blood flow to the tumor was redetermined with color

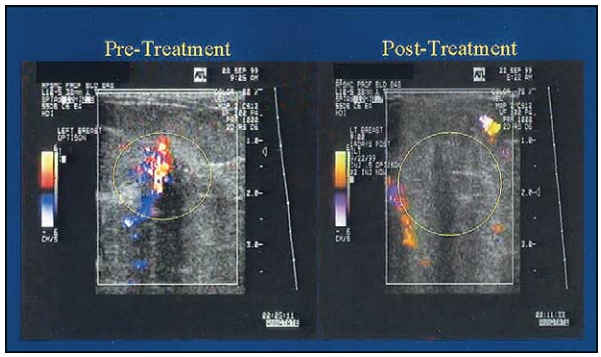

Fig. 3. Tumor blood flow before and after laser treatment of a breast cancer.

Doppler ultrasound prior to excision (Fig. 3). Two patients, 1 with recurrent breast carcinoma after lumpectomy and radiation therapy 3 years earlier, refused further surgery. They were treated with interstitial laser and were followed up with mammography and ultrasonography.

Results

Demographic data of 54 patients with invasive (n = 50) and in situ (n = 4) breast cancers initially treated with interstitial laser and surgically removed 1 to 8 weeks later for pathological evaluation are shown in Table 1. None of the patients sustained any systemic adverse effect and there was no incidence of hematoma or infection after laser therapy. In two instances, small (4 × 3 mm) skin burns occurred during the early phases of our experience. The treatment time ranged 25 to 30 minutes. Pathology of the laser-treated tumor revealed a 2.5 to 3.5 cm hemorrhagic ring surrounding the necrotic tumor (Figs. 4 and 5). The overall success rate for complete tumor ablation was 70%. This includes learning phase, technical and procedural changes implemented over 7-year period as summarized in Table 2. However, under steady conditions, in two groups of 14 patients, 93% and 100% of the tumors showed complete necrosis, with no residual cancer (clear margins) noted. The 2 unresected cases with 10-mm and 7-mm breast cancers were

Table 1
Demographic data of 54 patients with early breast cancer treated with laser therapy

Period of study	November 1994 to October 2001
Number of patients	54
Age, years (median)	42–80 (60)
Tumor diagnosis	
Invasive ductal	42
Invasive lobular	8
Ductal carcinoma in situ	4
Tumor diameter, mm (median)	5–23 (13)
Laser energy, joules	2,500–14,000 (5,900)
Diameter of necrosis, mm	10–32 (17)

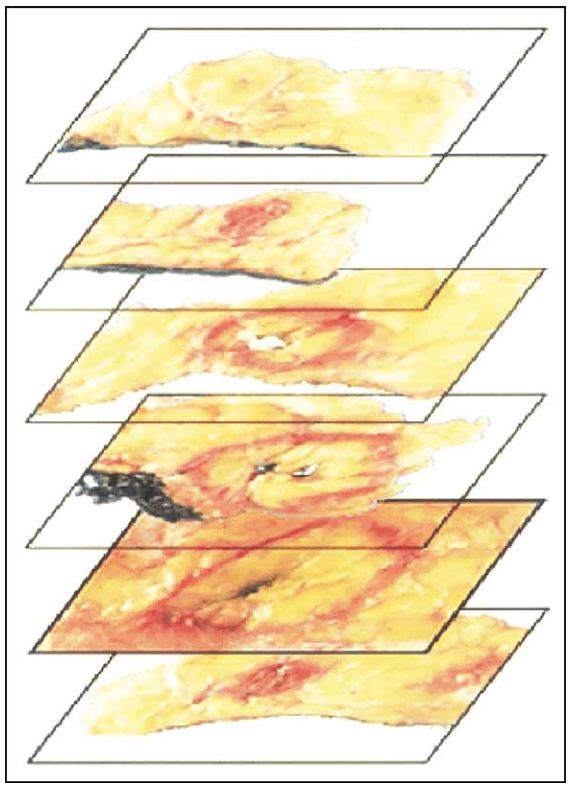

Fig. 4. Serial 2-mm sections of a laser-treated breast cancer.

closely followed up for 6 and 24 months respectively. Initially a soft (3 × 4 cm) mass was palpated at the site of the laser-treated tumors lasting up to 3 months and then gradually becoming impalpable. Patients experienced minimal aching sensation during the first week after therapy. Mammographically at 1 month the tumor outline became indistinct and needle core biopsy showed inflammation with early fibrosis. At 6 months a cyst began to develop at the

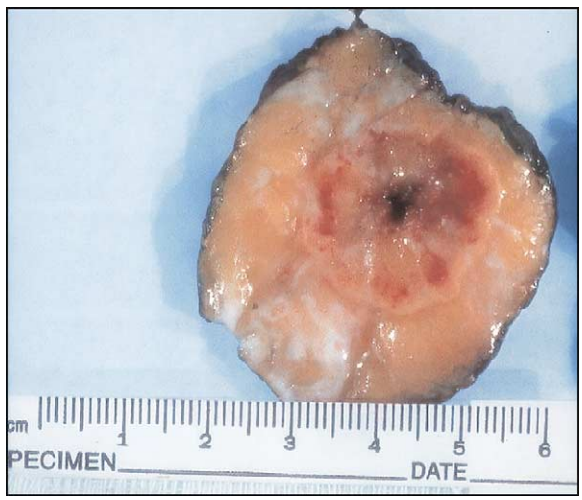

Fig. 5. Cross section of a lumpectomy specimen showing concentric rings of fat necrosis and hyperemia surrounding the centrally located 8-mm necrotic cancer after 4 weeks.

Table 2
Analysis of 16 patients with residual tumor after laser therapy

Number of patients	Comments
4	Inadequate laser energy (learning phase)
2	Oversedated patients, involuntary motion
4	Technical failure: malfunctioning thermal probes (3), fluid pump (1)
5	Suboptimal target visualization: excessive fluid infusion (3), hematoma post-needle biopsy (2)
1	Large tumor (2 cm)

treatment site and became mature at 18 months. This cyst was drained showing acellular debris. Its wall thickened at 24 months. Both patients remained free of pain and breast deformity during this period of observation (Fig. 6).

Comments

Detection of small breast cancers by annual screening mammography and application of image-guided needle biopsy devices have significantly changed the approach to diagnosis of breast cancer. These devices include vacuum-assisted needles and automated cannulae that allow the physician to remove large volumes of the suspicious tissue and increasingly the entire target [6–9]. Thus, percutaneous diagnostic needle biopsy of small breast cancers is approaching therapy. In-situ ablation of these tumors by freezing or heating may also prove effective for breast cancer as it has been the case in other solid organs. Cryotherapy and radiofrequency of liver metastases, prostate and breast cancer have been reported [10–18]. Application of laser energy for coagulation of breast tumors via an optic fiber is an appealing concept, which has been successfully tested for ablation of hepatic and palpable breast tumors [19–21].

The introduction of stereotactic technology in the United States in 1986 allowed physicians to diagnose occult breast tumors [22,23]. The use of this technology for delivery of ablative laser energy to the target tumor is the logical extension of this development. Our group initiated and tested the technique in the laboratory on chemically induced rodent mammary tumors [24]. It was noted that tumors heated to 60°C were completely destroyed. This observation was subsequently tested on patients with liver metastases with no systemic adverse effect on patients. Other investigators also reported similar findings [19,20].

We have previously reported our experience with 36 patients diagnosed with invasive and in-situ carcinoma [2,3]. Over the past 7 years we have made several changes in order to deliver the laser energy to the targeted tumor more efficiently. One of the reasons for failure leading to posttreatment residual cancer was inadequate visualization, which was noted to occur after injecting anesthetic fluid around the tumor (Table 2). We overcame this problem by inserting metallic markers around the tumor before infusion of anesthesia.

Real-time coagulative changes of the tumor during laser therapy are not detectable by digital images. However, continuous recording and display of the tumor temperature centrally and peripherally have helped us to determine the adequacy of treatment. The end point is reached when all the peripheral temperatures record 60°C. Contrast enhanced color Doppler ultrasound post-laser therapy delineates the loss of blood flow to the tumor as shown on Fig. 3.

Interstitial laser therapy has the potential to change the paradigm for local treatment of mammographically detected well-defined breast cancers. It is a less invasive alternative to open surgery for a subset of mammographically detected breast tumors. Indeed it is the logical extension of the image-guided breast biopsy widely practiced in the United States. Currently, there are more than 2,000 stereotactic tables installed at various medical centers in the United States and more than 6,000 surgeons and interventional radiologists trained in its use. Implementation of percutaneous laser therapy of such tumors requires minimal additional training. By providing a virtually pain-free treatment without tissue removal, in-situ ablation of breast cancer is an appropriate treatment for mammographically detected breast cancers.

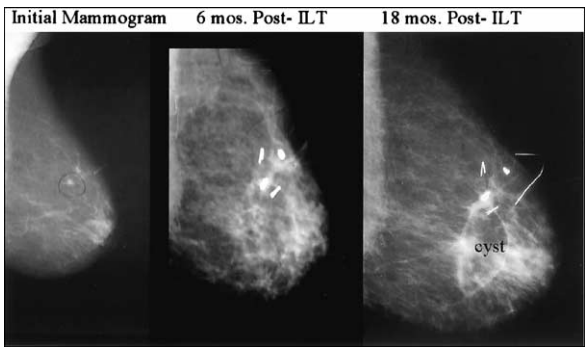

Fig. 6. Mammographic temporal changes of a laser-treated breast cancer showing an oil cyst formation.

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