Lasers in Surgery and Medicine 26:467–476 (2000)

Temperature Mapping of Magnetic Resonance-Guided Laser Interstitial Thermal Therapy (LITT) in Lymphangiomas of the Head and Neck

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Background and Objective: **Lymphangiomas of the tongue and neck are uncommon benign congenital lymphatic tumors. These vascular lesions are difficult to treat, frequently recur, and can cause patients significant morbidity. Treatment may also be complicated by adjacent vital anatomic structures. Magnetic resonance (MR)-controlled laser-induced interstitial thermotherapy (LITT) has been proven to be a non-invasive safe treatment. Real-time monitoring of tissue temperature with thermosensitive sequences allows controlled coagulation necrosis.**
Study Design/Materials and Methods: **LITT was performed in a lymphangioma specimen ex vivo. In four patients (eight procedures) with lymphangiomas of the tongue and neck, MR-guided LITT was performed with a percutaneous approach in a multiapplicator technique. The laser system consisted of a titanium catheter and a protective catheter. The dome of the fiber end had a diameter of 1.4 mm with an active length of 20 mm. Temperature sensitive sequences were used in a 0.5 T open-configured MR scanner with the proton frequency shift technique to map the spatial and temporal distribution of Nd:YAG laser effects (7 Watts, 30 pulses per second, 10 minutes/location). Postoperative MR follow-up was performed at 1 week and at 3 months. In three patients, partial resection of the tumor was performed 6 months after LITT.**
Results: **In three patients, MR clearly showed a diminished tumor volume. All four patients reported subjective amelioration and in three patients former functional problems, such as speech and swallowing were improved. MR thermometry allowed accurate demarcation of changes by heat and distinction of affected tumor volume (3.0 cm ± 0.3 cm). The histology of the patients 6 months after LITT showed laser-induced fibrosis of former lymphatic tissue.**
Conclusion: **The results suggest that LITT can be performed safely with tissue preserving of vital structures and can be effective in the treatment of deep tumors, such as lymphangiomas. However, given the nature of the lesion, the potential for recurrence exists no matter what modality is chosen. Lasers Surg. Med. 26:467–476, 2000.**
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Key words: head and neck neoplasms; lasers; laser tissue interaction; MR thermometry; tissue temperature measurements

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Accepted 13 January 2000

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INTRODUCTION

Lymphangiomas are a rare, benign congenital tumor of the lymphatic system. Eighty percent of these tumorous lesions are usually found before the age of 2 years [1] and rarely occur in adults [2]. Approximately 75% percent occur in the cervical region [1]. According to Mulliken and Glowacki [3] vascular lesions are distinguished in two major categories: hemangiomas and vascular malformations. Vascular malformations are subdivided into venular dermal, venous, lymphatic, and mixed. Therefore, lymphangiomas also may be designated as lymphatic or mixed vascular malformations. It is important to understand embryology of the lymphatic system, which describes the lymphatic system as an out-growth of the venous system [4]. Two basic theories, the centrifugal [5] and the centripetal [6], have been established. However, lymphangiomas represent areas of regional dilation of lymph channels [7] and, therefore, are distributed histologically into lymphangioma simplex (capillary), cavernous and cystic [8]. Patients with cervical lymphangiomas may complain about functional problems, such as speech and swallowing difficulties or stridor, but also pain is experienced by some of the patients. Complete surgical resection of the more complex lesions carry with it the possibility of damaging vital structures [1]. Also because of the lack of the well-defined visible or palpable margins, lymphangiomas are frequently incompletely excised [7].

Laser-induced interstitial thermotherapy (LITT) is a technique for localized tissue damage, especially in deep-seated tumors. Due to tissue temperature, effects may differ from malignant cell necrosis (41–44°C] (laser-induced hyperthermia, LIH) up to irreversible tissue damage by denaturation of proteins(>60°C) or carbonization (>100°C). We hypothetically suggest, that a temperature rise of 60°C resulting in coagulation necrosis initiates transformation of lymphatic tissue into fibrosis. Lasers used for LITT are typically high-power continuous wave, near infrared lasers such as the Nd:YAG (1,064 nm) or diode lasers (850 nm) [6,7]. Near infrared lasers are characterized by high transmission characteristics. The Nd:YAG laser has become the standard tool for LITT; hence, diode lasers also have proven to be effective in LITT while providing several advantages [9]. Application of laser energy by an optical fiber probe inserted into the body requires guidance by imaging for proper anatomic positioning. Not only insertion, also tissue temperature rise during lasing needs to be observed when vital anatomic structures are in close vicinity to tumorous structures.

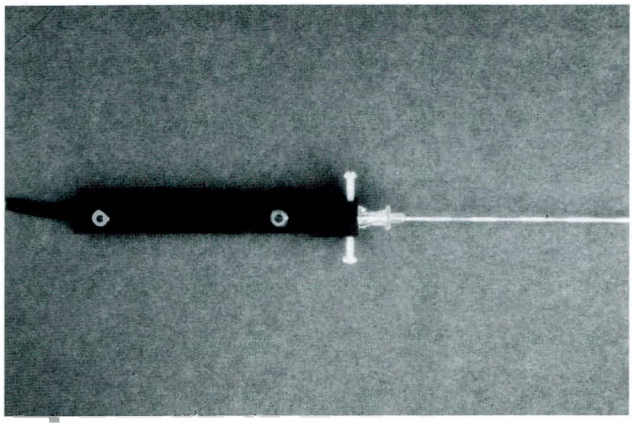


Fig. 1. A stereotactic biopsy system with needle holder allowing real-time control of the needle placement. Two diodes on the needle holder emit infrared signals, which are detected by three cameras in the ceiling of the magnetic resonance system.

Tissue changes generated by LITT may be measured with MR, computed tomography, or ultrasound postoperatively. Temperature sensitivity inherent to MR experiments provides the basis for use of MR-imaging to monitor thermosensitive therapies [10]. Direct patient access is provided by a midfield (0.5 Tesla) superconductive, open-configured MR system. This MR system enables the integration of diagnostic imaging, tumor localization, and monitoring of tumor laser therapy. Real-time MR monitoring (thermosensitive sequences) of tissue temperature allows controlled coagulation necrosis during treatment.

MATERIALS AND METHODS

Laser and Fiber-Optic Probes

An Nd:YAG laser (1,063 nm) unit (Excel, Darmstadt, Germany) was positioned outside the interventional MR suite. A long laser fiber (12 m long) linked the laser to a specially designed connecting box situated at the scanner itself. A fiber, LITT standard applicator (A13-0539) (Hüttinger, Umkirch, Germany), was plugged into the Nd:YAG laser for lasing. The dome is characterized by the following parameters: diameter of the dome 1.4 mm, length of the dome 30 mm with an active length of 20 mm. In all interventions, an Nd:YAG laser was set to a constant power output of 7 W for 10 minutes with 30 pulses per second.

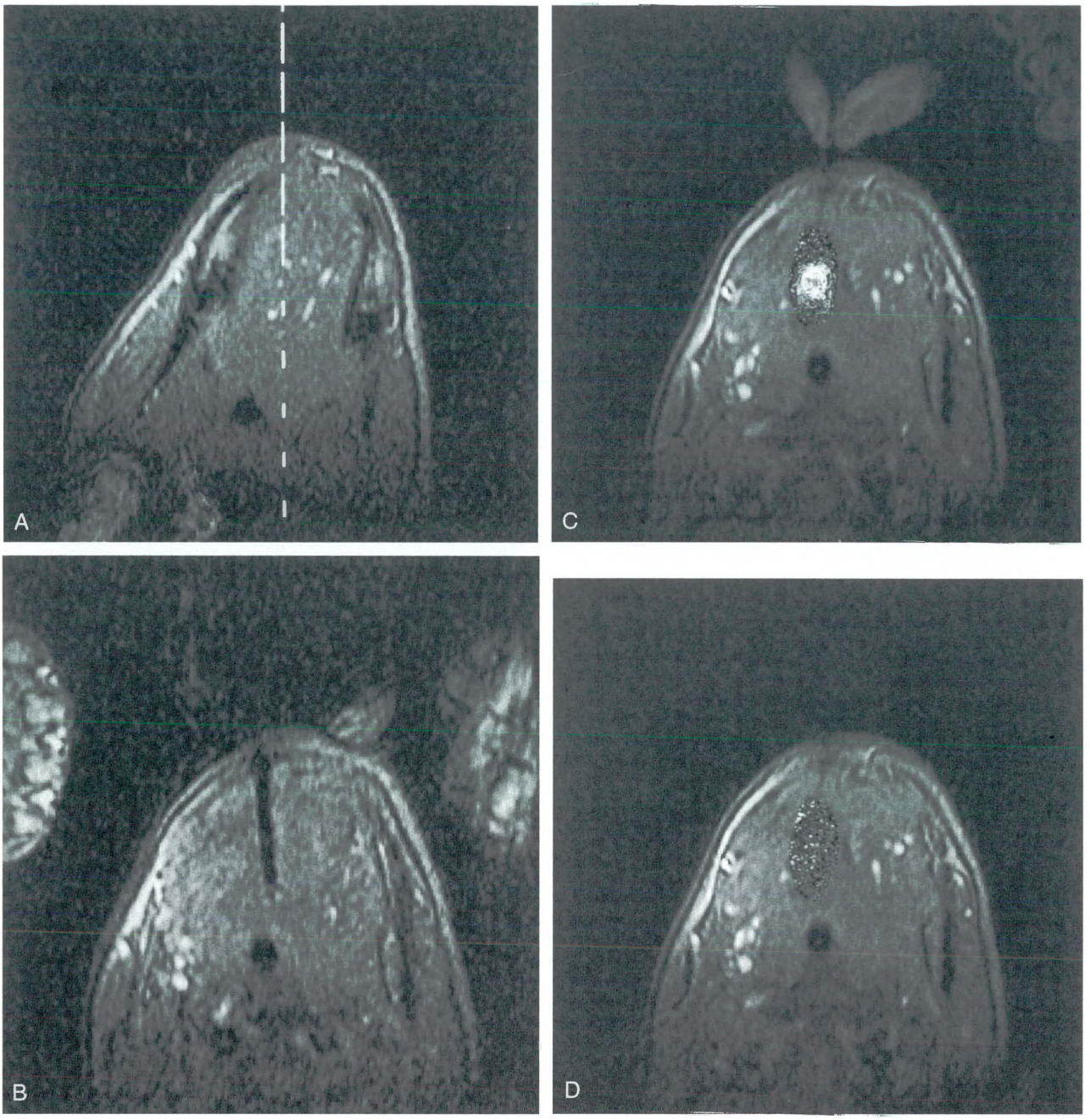


Fig. 2. **A:** Magnetic resonance (MR) imaging of a lymphangioma in the floor of the mouth and tongue in a 0.5 Tesla open-configuration, interventional MR system. The computed needle trace is integrated on the real-time image as a white dotted line. **B:** Placement of the catheter. **C:** Color-coded visualization in a real-time MR image obtained 5 minutes after initiation of lasing. The step of colors corresponds to 5°C. Only temperature (phase) changes were displayed. Note the fingers of the operator holding the protective catheter and the fiber. **D:** Color-coded visualization in a real-time MR image obtained 5 minutes after termination of lasing.

Before open MR procedures, the laser system and settings were used in a lymphangioma specimen.

MR Imaging

All imaging was obtained on a 0.5 Tesla super-conducting, open-configuration MR-system (Signa SP; General Electric Medical Systems, Milwaukee, WI). A 58-cm-wide gap in the magnet is freely accessible by the interventionalist. Flexible surface coils are used for radio frequency (RF), signal transmission, and reception.

To provide a morphologic roadmap, axial T1-

weighted spin echo images (TR/TE 500/20, 8-mm sections) were acquired. A 24-cm field-of-view (FOV) and a matrix of 256 × 128 rendered an in-plane resolution of 0.9 × 1.8 mm. Temperature-sensitive imaging was based on a gradient echo sequence by using the following parameters: TR/TE 19/9 msec, flip angle 30 degrees, bandwidth 16 kHz. Imaging plane, section thickness, FOV, and matrix were chosen to coincide with the morphologic roadmap image. Temperature sensitivity of the gradient-echo sequence is based on temperature-dependent alterations of the spin lattice relaxation time T1 and equilibrium magnetization. Initially, one temperature-sensitive gradient-echo image (acquired before initiation of lasing) was transferred to a SPARC-10-workstation (SUN Microsystems, Mountain View, CA) as a baseline reference image. After initiation of lasing, all subsequent gradient-echo images were automatically transferred to the workstation and subtracted from the baseline reference image. The resulting subtraction image displayed signal changes induced by the laser application. These differences were color-coded and projected on the morphologic spin-echo roadmap image. The temperature-sensitive images were updated every 3 seconds. The software rendering color-coded temperature-sensitive MR images was developed at our institution. The tissue volume affected by laser energy was estimated in thermosequences.

LITT in Four Patients

Informed consent was obtained by four patients (2 male, 2 female; 4, 8, 25, and 38-years old) with a radiographically and histologic confirmed cystic lymphangioma of the neck and tongue, who agreed to undergo LITT under MR guidance and control in the open-configuration MR system. A 10-cm-long and 2.7-mm-wide, needle of titanium alloy (Sumatex, Berlin, Germany) was introduced stereotactically into the tongue and the submandibular region of the neck. All patients were treated in more than one location (one patient was treated once, two patients twice, and one patient with three interventions). For safe and accurate placement of the needle, a stereotactic needle positioning system (Flashpoint 5000; Image Guided Technologies, Boulder, CO) was used (Fig. 1). The orientation of the real-time imaging (updated every 3 seconds) can be automatically adapted to the needle orientation. Once the needle was placed in the tumor, the laser fiber was introduced into the protective catheter and temperature-sensitive imaging was commenced. During lasing, tempera-

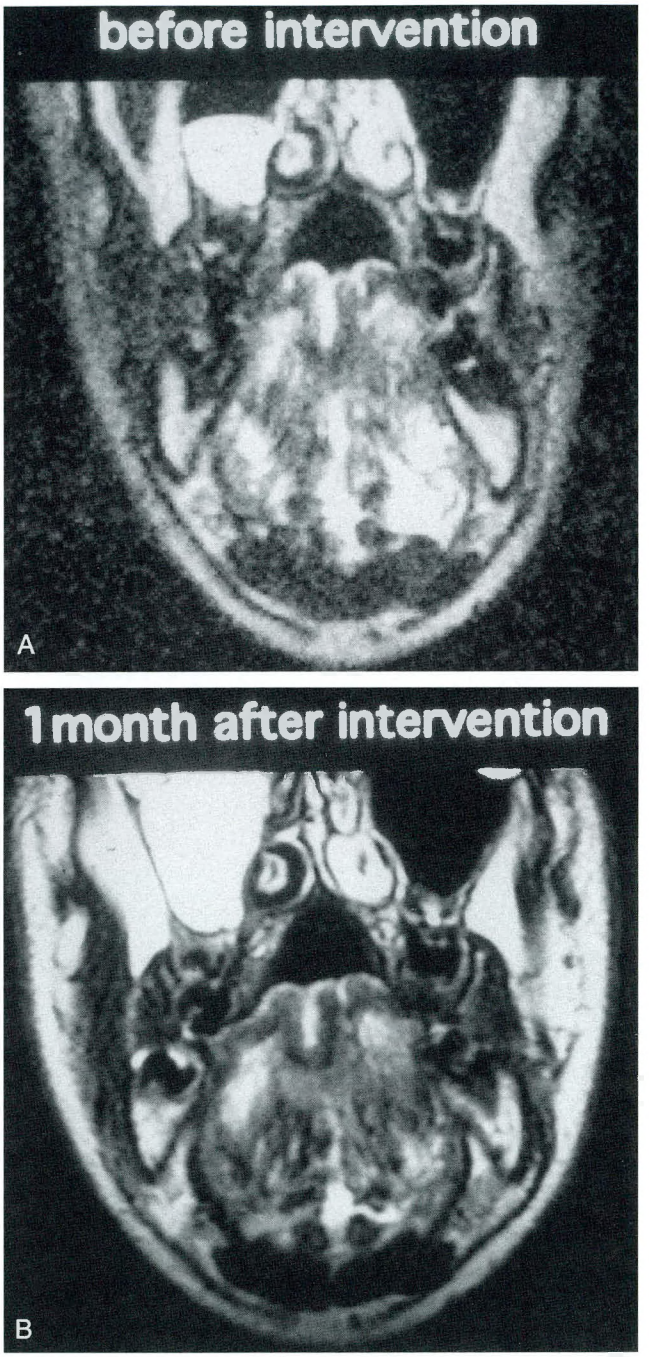


Fig. 3. **A:** Coronal T2 weighted magnetic resonance (MR) image of a lymphangioma in the floor of the mouth and tongue (same patient shown in Fig. 2) before laser-induced interstitial thermotherapy (LITT). Signal enhancement in the base of the tongue on the left side of the patient showing the lymphangioma. **B:** Coronal T2 weighted MR image 1 month after LITT, showing a significant decrease of signal in the left base of the tongue.

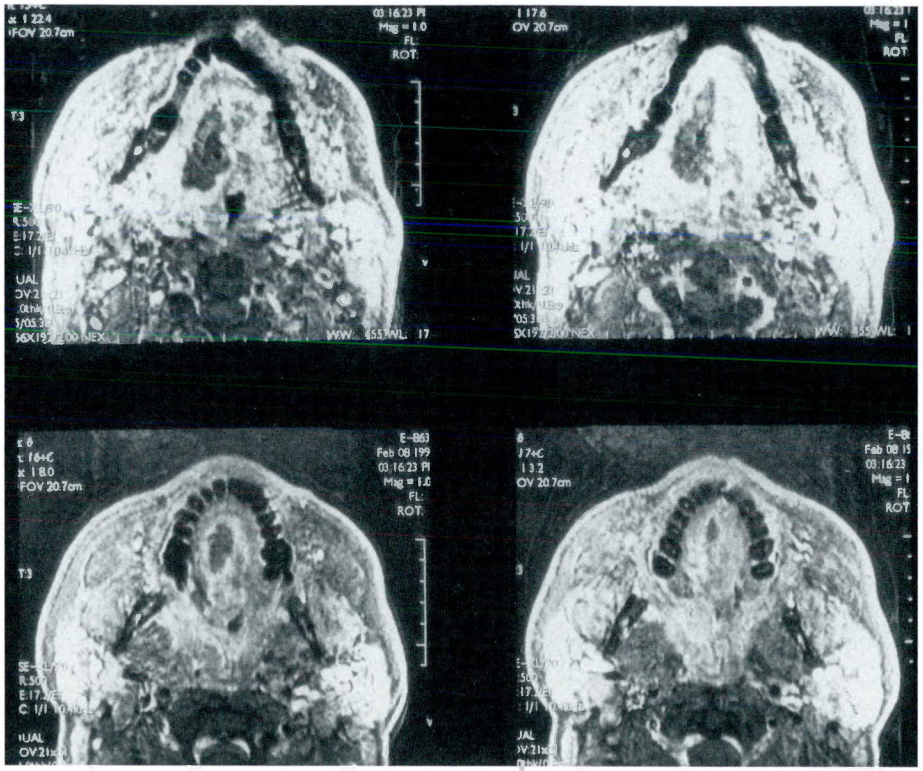


Fig. 4. Four Axial T2 weighted magnetic resonance images of a lymphangioma in the tongue 1 week after laser-induced interstitial thermotherapy. Note the coagulation necrosis, present as a hypovascular area extending from the base of the tongue to the back of the tongue.

ture-sensitive, color-coded gradient-echo images were acquired every 3 seconds.

Histology

Temperature damage was studied in lymphangioma tissue after LITT ex vivo. The treatment concept for tongue lymphangiomas also consisted of a partial resection of the tumor, so that the laser effects could be studied in specimens after LITT in vivo in four patients. The preoperative sections were compared with changes 6 months postoperatively.

RESULTS

Coagulative necrosis was achieved in all four patients. Also clinical symptoms were reduced in all four patients.

Under general anesthesia and MR guidance with the Flashpoint system, optimal positioning of the cannula and mandrin was achieved in all patients (Fig. 2A,B). After the protective catheter had been positioned, and the laser tip had been inserted, the laser energy was delivered through the fiber (Nd:YAG laser, 7 W, 10 minutes with 30 pulses per second) and monitored with the color-coded sequence (Fig. 2C,D). Minimal carbonization or vaporization of tissue in vicinity of the dome (1 mm) was observed. No damage of equipment occurred during the treatment. MR follow-up showed a zone of coagulation necrosis and edema in all four patients immediately after surgery and 1 week postoperatively. The size of the lesion was significantly diminished at 3 months postoperatively (Fig. 3A,B). Especially the size of the characteristic lymphatic cysts decreased.

MR thermometry enabled on-line display of hyperthermic effects, which were seen in all patients as an area with progressively decreasing signal intensity that surrounded the laser-emitter tip. In all four patients, laser-induced temperature changes resulted in signal alterations, which were displayed in color-maps on the morphologic images. Color changes generally appeared 2–3 minutes after initiation of lasing. Temperature spread during lasing was visualized by a growing extension of the color focus. After termination of lasing, the color spread decreased in size. Calculated tissue necrosis showed a volume range of 2–3 cm (Fig. 4).

Coagulation necrosis induced by an Nd:YAG laser has been measured in a lymphangioma specimen in vitro providing reasonable diameters (Nd:YAG laser, 7 W, 5 minutes). The histology clearly showed the tissue damage attributable to the distance of the emitting laser probe (Figs. 5–7).

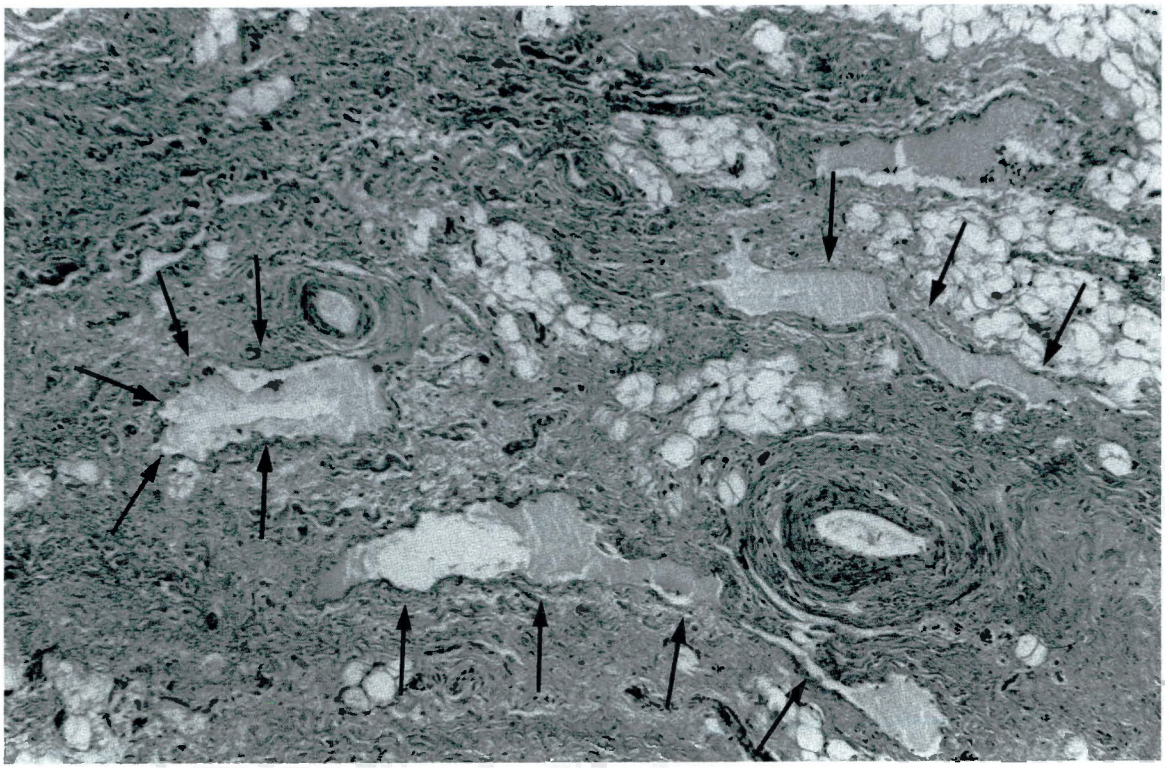


Fig. 5. Elongated lymphangiomatous vessels are visible between soft tissue and fat lobules (arrows). Hematoxylin and eosin stain; original magnification, ×30.

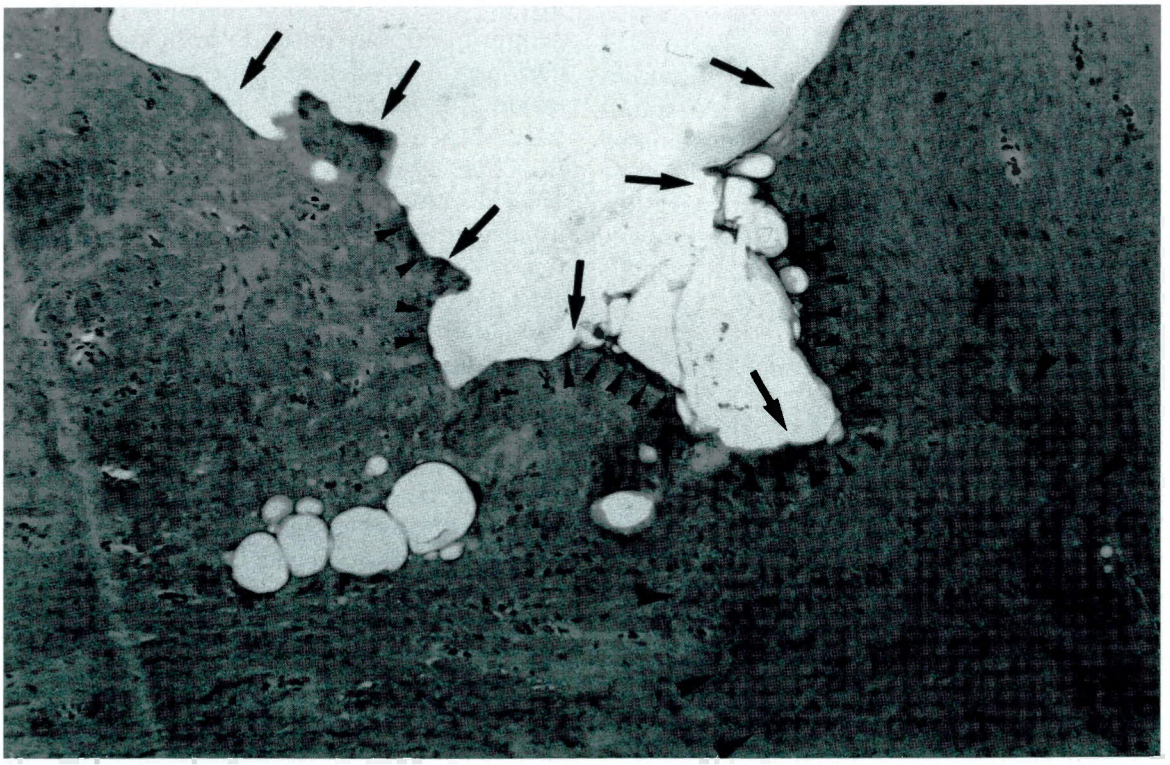


Fig. 6. Laser-induced tissue defect shows irregular contour (arrows). Adjacent tissue shows a narrow seam of carbonized tissue (small arrowheads) and a broad zone of hyalinization (large arrowheads). Elastin van Gieson stain; original magnification, ×160.

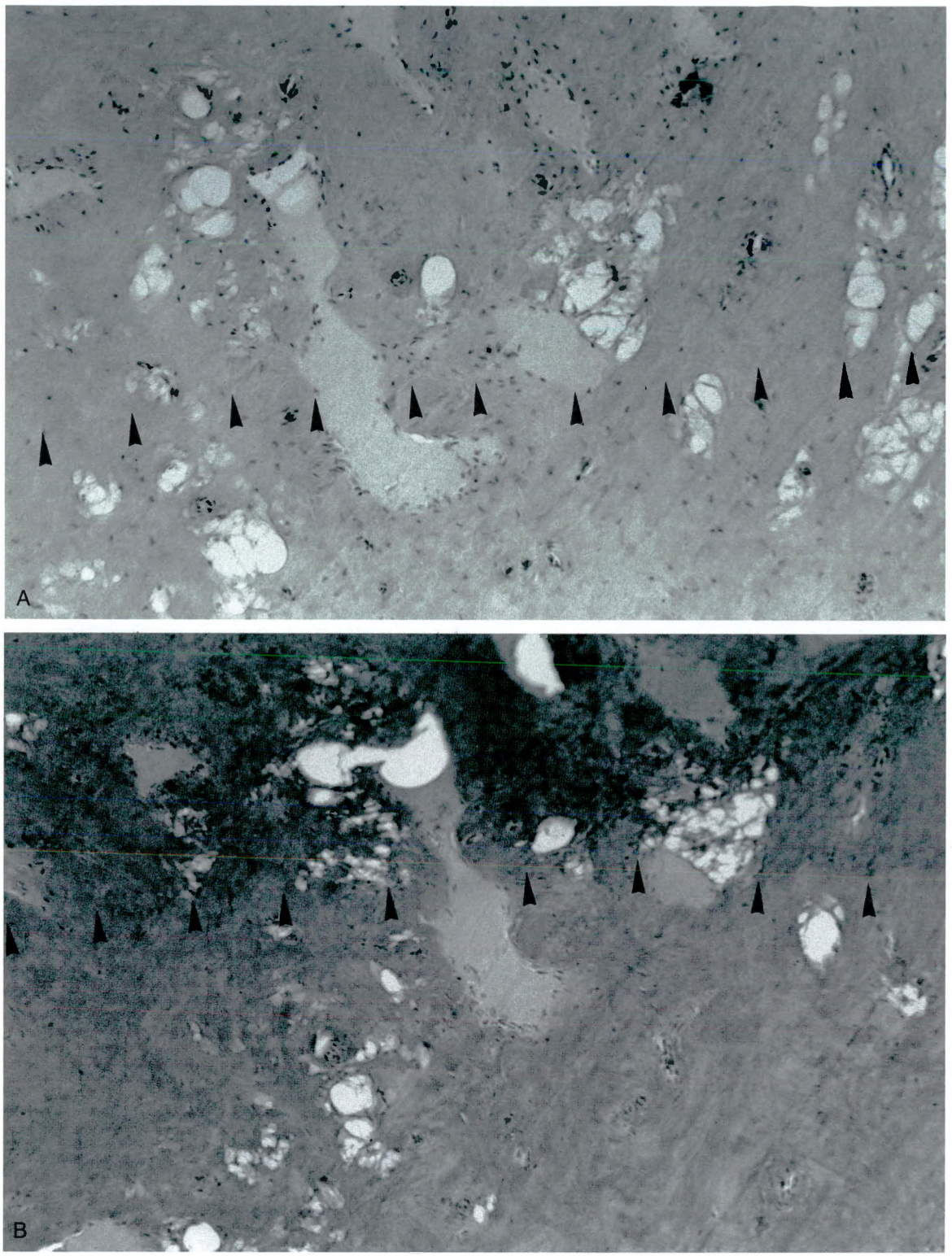


Fig. 7. These images show transition of a coagulation zone of soft tissue to the broad area of hyaline change (arrowheads). Hematoxylin **(A)** and eosin and elastin van Gieson **(B)** stains; original magnification, ×160.

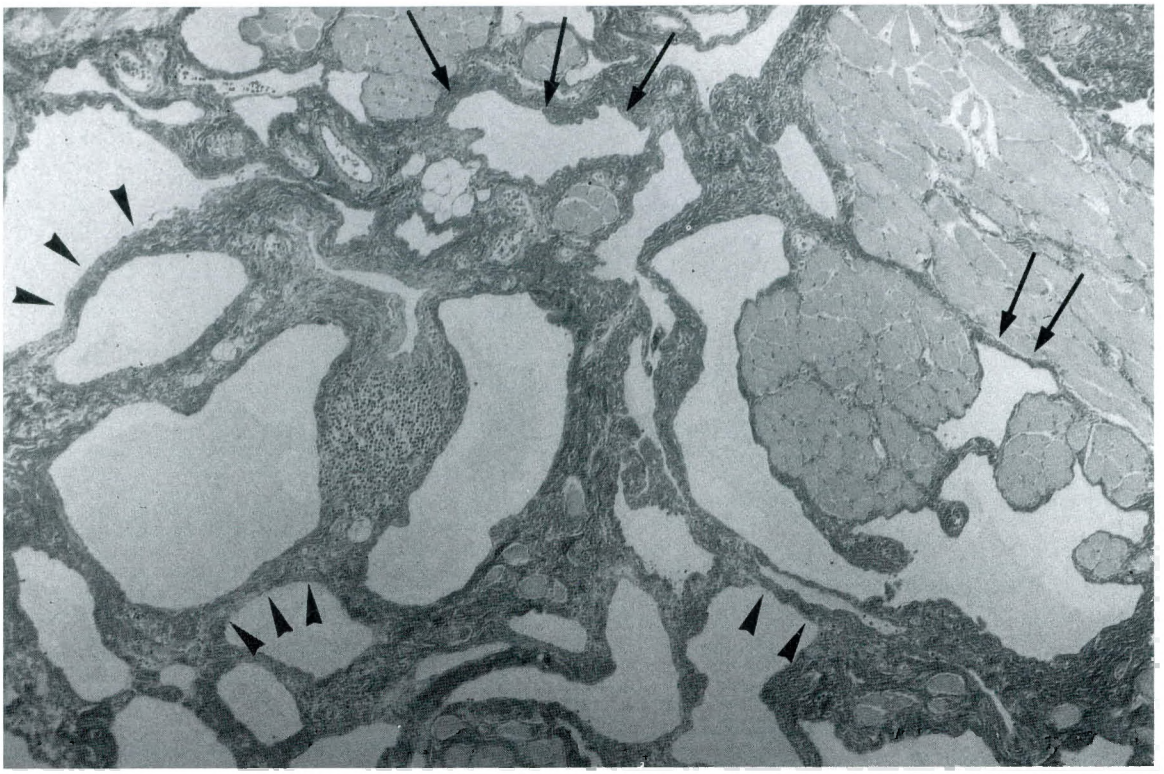


Fig. 8. Large cavernous spaces of lymphangioma surround and dissect between the tongue skeletal muscle fibers and soft tissue (arrows). Note the slender septae between the lumina (arrowheads). Elastin van Gieson stain; original magnification, ×50 Prelaser biopsy.

In four patients, a partial resection of the tongue was performed for functional reasons (macroglossia) 6 months after lasing. Histologic investigation revealed fibrotic changes of tissue. Lymph channels or smaller multiloculated fluid filled cysts lined by flattened epithelium were surrounded by masses of fibrotic connective tissue (Figs. 8, 9).

DISCUSSION

The Nd:YAG laser at 1,063 nm has been recommended as an efficient tool for LITT in different tissues [11]. Also, diode lasers have been recommended for LITT [9]. However, most studies performing LITT in vascular lesions used the Nd:YAG laser [12]. Because of the absorption coefficient and transmission characteristics, the Nd:YAG laser [13] may be superior in treatment of hemangiomas and lymphangiomas (endothelial structures) compared with the diode laser. We are favoring pulsed versus continuous energy, assuming that pulsed energy causes less charring next to the fiber while achieving a similar temperature rise in the tissue. Large carbonized tissue volume in deep-seated tumors is hardly catabolized and may cause abscess formation. However, tissue changes are mainly based on thermal damage. Our results are introducing the Nd:YAG laser as a good tool in LITT of lymphangiomas.

LITT of deep-seated tumors is a new technique for lymphangiomas that are not completely operable. Energy doses deposited within the tumor by using LITT can be high enough to damage the surrounding healthy tissue. For a clinically effective control of LITT, a reliable, quantitative temperature monitoring is, therefore, of great importance. To date, tumor puncture and the subsequent thermal procedure is commonly performed under ultrasound or computed tomographic control without any temperature information. With the availability of interventional MR scanners these limitations can be overcome to a great extent. Open MR scanners allows MR-guided targeting of tumors, as well as continuous monitoring of temperature propagation during the subsequent thermal procedure. Quantitative temperature monitoring of LITT can be demonstrated in a 0.5 Tesla open-configured MR scanner with proton frequency shift technique. Compared with

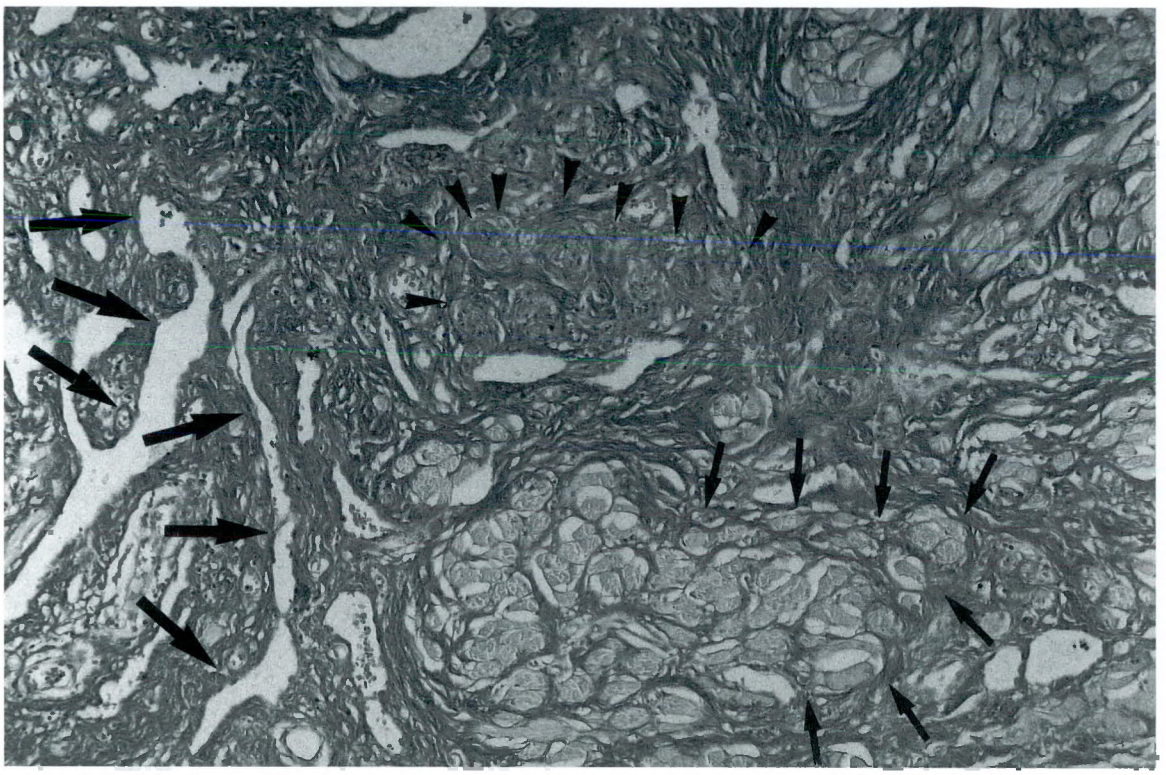


Fig. 9. This postlaser biopsy of a similar region from a different patient after laser coagulation of a lymphangioma shows focally massive soft-tissue fibrosis with encasement of skeletal muscle fibers (arrows). There is also focal reactive proliferation of blood vessels (arrowheads). Note the slender lumina of angiomatous spaces (large arrows). Elastin van Gieson stain; original magnification, ×80.

conventional 1.5 Tesla MR scanners, the advantage of free patient access and image-guided targeting had to be paid with lower field strength and a lower temperature sensitivity [14].

Lymphangiomas of the tongue and neck are rare congenital lesions of the lymphatic system. Several reports of this interesting condition have appeared in the literature with varying modalities of treatment, including surgery, radiation, injection of sclerosing agents and corticoid, aspiration, and laser treatment [15,16]. To control the size of the tumor for functional reasons, especially in the tongue, surgical resection is the method of choice [17,18]; although, tumors are often adherent to adjacent vital structures such as the thyroid gland, and carotid sheath, cranial nerves, or major vessels of the neck [18]. Considering that lymphangiomas are benign lesions, tissue preserving techniques, such as LITT, are favorable in close vicinity to vital structures. Suen and Waner [12] reported excellent responses in six patients with vascular malformations of the oral cavity, by using an Nd:YAG laser. Our series of four patients demonstrates improvement of function after LITT. Moreover, MR follow-up documents macroscopic changes. Fibrosis induced by thermal damage has been shown by histology. Because complete removal cannot always be achieved, multiple and combined intervention strategies are necessary. Recurrence of symptoms appeared in only one case, requiring repeated surgical interventions.

The results suggest that LITT can be performed safely with tissue preserving of vital structures under on-line MR monitoring in deep tumors such as lymphangiomas. Overall, the data presented suggest that an Nd:YAG laser can be recommended for use of LITT to treat this type of lesion. However, given the nature of the lesion, the potential for recurrence exists no matter what modality is chosen.

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