

Laser thermal ablation in multimodality treatment of liver metastases from neuroendocrine tumors



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Liver metastases (LM) from neuroendocrine tumors (NET) occur with variable frequency depending on the primary disease, ranging from 5-10% for carcinoid to 75% for glucagonoma¹. LM have a major impact on survival, and the relatively indolent nature of well-differentiated NET and their proclivity to be hormonally active warrant aggressive treatment even for advanced stage disease. Systemic medical therapy is marginally effective in NET, and aggressive cytoreduction using combined multimodality treatments such as surgery, transarterial chemoembolization, and thermal ablation, can improve both survival and quality of life. The reported 5-year survival of patients with LM from NET treated medically ranges from 0 to 30%. In contrast, aggressive cytoreduction has been reported to achieve 5-year survival rates ranging from 48 to 83%^{1,2}, and many guidelines for the management of NET recommend the removal of at least 90% of LM whenever possible^{2, 3,4}. To this aim, surgical resection is considered the gold standard, but only 10-20% of patients with NET are actually candidates for resection because the disease is too extensive. Moreover, the 5- and 10-year recurrence rates after resection are 84% and 94%, respectively, with a median time to recurrence of 21 months¹. Consequently, the need of frequently retreating the patients makes less invasive methods of aggressive cytoreduction a quite interesting option. Image-guided thermal ablation offers the possibility of a minimally invasive technique that is usually associated with less morbidity than

resection, decreases tumor volume, preserves most of the normal liver, and can be repeated several times.

Ablative therapies can be used in place of or as an adjunct to resection. In brief, they can preferentially be used for deep small lesions (diameter less than 4 cm) and recurrent lesions, and they can be considered as an adjunct to resection in patients with extensive bilobar disease. In this regard, Elias et al reported a 3-year survival rate of 84% in 16 patients with a median of 23 LM per patient, treated with surgical resection combined with intraoperative radiofrequency ablation⁵.

Thermal ablative techniques can deliver thermal energy, either cooling (the so-called cryoablation) or heating the tissue. Radiofrequency ablation (RFA), microwave ablation (MWA), and laser ablation (LA) enable to raise the temperature of the tissue between 60° and 100°C, producing coagulative necrosis. RFA has largely become the dominant ablation modality, and is extensively used worldwide to ablate both primary and metastatic liver tumors. However, MWA offers some advantages over RFA, including higher intratumoral temperatures, deeper penetration of energy, propagation across poorly conductive tissues, and larger ablation volumes⁶. Moreover, the development of a miniaturized device for MW confinement has recently enabled to minimize the well-known and undesired back heating effects, using slender MW antennas than conventional MW systems. In a prospective pilot study, we demonstrated that this new MWA system can achieve significantly larger ablation areas than RFA, using antennas with a diameter comparable to that of the internally-cooled RFA needle electrode⁷. LA, according to the technique proposed by Pacella⁸ and improved by Di Costanzo⁹, uses 300 µm bare optical fibers introduced into the tumor through 21-gauge needles. The diameter of the needles is quite smaller than RFA electrodes and MWA antennas, making LA safer and more suitable to ablate lesions with at-risk location and/or difficult to be reached. Moreover, the use of a multi source device, that allows the use of up to four fibers at once, and the pull-back technique, enable to produce thermal lesions up to 4-5 cm in diameter.

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In our Section of Interventional Ultrasound, all of these three thermal ablation systems are available, so we can plan the treatments tailoring the best ablation technique on each single patient, according to the number, size and location of the lesions. RFA is the first technique we implemented, and our experience is long-lasting, with very good results in terms of both technical success and long-term outcome, especially in nodules up to 3 cm in diameter. However, in the last years RFA is going to be replaced by MWA in presence of large lesions (over 3 cm in diameter) and lesions located close to vascular structures, as MWA is less influenced by the sink-effect than RFA. The possibility of placing from one to four fibers into the tumor makes LA the most flexible ablation technique. A bare-tip fiber provides an almost spherical thermal lesion of 12-15 mm in diameter, and the lesion size can be increased up to 4-5 cm by using multiple fibers with the pull-back technique. In our opinion, such a peculiarity makes LA the ablation technique of choice in presence of multiple liver tumors of different size. Using from one to four fibers, it is possible to tailor thermal lesion size on nodule size, obtaining an acceptable safety margin in tumors ranging from 5-6 mm to 3-4 cm in diameter, contemporaneously sparing the normal parenchyma as far as possible.

LM from NET are frequently multiple, small and variable in size, and very slow growing. Therefore, it is possible to treat patients with indolent disease with very numerous and small (≤ 3 cm) LM, even at multiple treatment sessions over a period of years¹⁰. Because of its peculiarities, in our Center LA, associated or not with other cytoreductive treatments such as surgical resection and transarterial chemoembolization, according to the decision of our multidisciplinary team, has become the standard ablation technique in this subtype of selected patients.

To date, we have treated 133 LM from NET at 28 sessions (range 1-5) in 13 patients (mean 10.2 ± 7.7 LM for patient; median 7 LM, range 3-28). Tumor size ranged from 5 mm to 35 mm. LA was performed under ultrasonography or contrast-enhanced ultrasonography

(CEUS) guidance using one bare-tip fiber for lesions up to 7 mm in transverse diameter; two fibers spaced 12-15 mm for lesions between 7 and 15 mm; three fibers spaced 12 mm each other for lesions between 15 and 20 mm, and spaced 15-18 mm each other for lesions between 21 and 35 mm. 1800 Joules in six minutes were delivered for each fiber, and the pull-back technique was always used when the anteroposterior diameter of the tumor exceeded 12 mm (see figures 1-4). No mortality occurred and one major complication out of 133 LA procedures was observed (0.75%): a bowel perforation in a patient who had previously undergone three abdominal surgical interventions for renal cancer, colon cancer, and carcinoid of the ileum.

Technical effectiveness, defined as a nonenhancing area with diameters equal to or greater than those of the treated tumors without any evidence of enhancing foci¹¹, and assessed by contrast-enhanced CT or CEUS performed one month after the procedure, was 100%. Six-month local recurrence was 5.3% (7/133); all the local recurrences were successfully retreated by CEUS-guided LA. At the time the data were censored (August 10, 2014), the median follow up period was 36 months (range 15-54 months). Four patients were dead because of hepatic

or extrahepatic tumor progression, 4 patients were dead for other causes, 3 patients were alive and disease-free, and two patients were alive with hepatic distant recurrences. LA has been planned for these two patients and it will be performed in the next months.

Even though our series is small and the follow-up is still too short to allow an evaluation of 3-year and 5-year overall survival, our results appear quite interesting and suggest that LA can represent a safe and effective option in the treatment of LM from NET. A multimodality approach is advocated because of the extension of the metastatic disease frequently encountered, and an aggressive cytoreduction aimed at achieving a reduction of at least 90% of the tumoral burden is recommended^{3,4,10}. To this aim, surgical resection, transarterial chemoembolisation, and ablative therapies are often associated, and in our opinion LA can represent the ablative technique of choice in this setting. Using a variable number of bare-tip fibers, it allows to tailor the thermal lesion on the size of each metastasis, balancing the need to obtain a good safety margin with the need of sparing normal liver parenchyma and preserving liver function as far as possible, as local recurrences are very frequent over the time and repeated treatments are frequently needed.

Fig. 1 – Contrast-enhanced sonogram of the left liver lobe showing a 14 x 12 mm thermal lesion obtained with one laser fiber

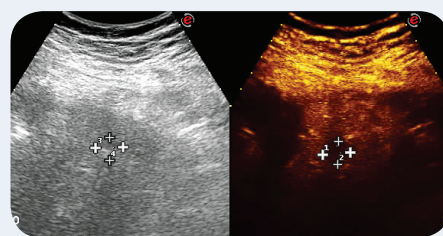


Fig. 2 - Contrast-enhanced sonogram of the right liver lobe showing a 26 x 31 mm thermal lesion obtained with two laser fibers and the pull-back technique

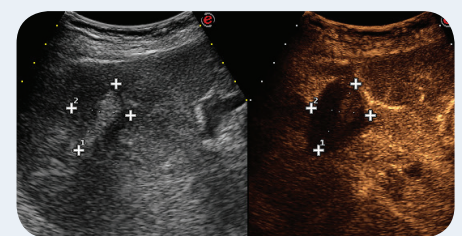


Fig. 3 - Contrast-enhanced sonogram of the right liver lobe showing a 34 x 20 mm thermal lesion obtained with three laser fibers

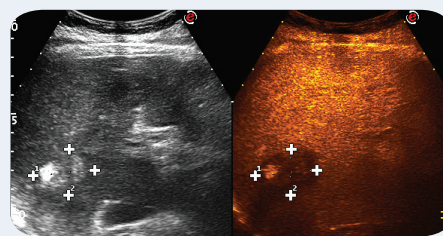
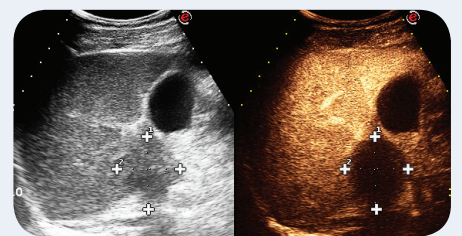


Fig. 4 - Contrast-enhanced sonogram of the right liver lobe showing a 38 x 44 mm thermal lesion obtained with three laser fibers and the pull-back technique



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Welcome to: Dr. Felicia Alexandra Hanzu, Dr. Mireia Mora, Dr. Mattia Squarcia for the innovative Clinical protocol regarding Percutaneous Laser Ablation (PLA) of Benign Thyroid Nodules



Dr. Felicia Alexandra Hanzu (afhanzu@gmail.com), **Dr. Mireia Mora**, Endocrinology Department, Hospital Clinic, Barcelona University; **Dr. Mattia Squarcia**, Radiology Department, Hospital Clinic, Barcelona University.

The Spanish Team started a very interesting Clinical protocol with a double target:

- **Verify the improvement in the quality of life after the PLA treatments**
- **Comparison between Costs of PLA and traditional surgery procedures.**

This protocol can be an example for everyone who wants to contribute to the diffusion of PLA procedures and to show the social convenience of PLA Minimally Invasive Therapy. Very important points in order to get the reimbursed protocol from the country local health organization.

Keywords:

Benign thyroid nodules; Percutaneous Laser Ablation.

Summary of structure:

(Rationale, Design, Trial subjects, Interventions, Tests to be conducted, Expected results)

Rationale:

Nodular thyroid disease, which has a high prevalence in the general population, requires prolonged ultrasound and analytical monitoring. In the case of malignant nodules as also benign compressive nodules sized ≥ 3 -4 cm or which significantly influence the patient's quality of life, the gold standard treatment is surgical.

These surgical procedures involve on one hand the costs incurred with any type of open surgery requiring general anaesthesia and hospitalisation, and on the other, the general risk of post-op complications and specific thyroid disease complications.

A minimally invasive technique called Percutaneous Laser Ablation (PLA) has recently been introduced in the clinical practice of benign no compressive but symptomatic nodules.

The initial trials conducted on small cohorts of patients who had contraindications to, or rejected surgery, reported significantly positive results with PLA in reducing the nodule volume and associated comorbidities.

Design:

Prospective, non-randomised pilot trial lasting 2.5 years. In the trial will be included 90 patients who have benign thyroid nodules with benign cytology, with a single thyroid nodule or a multinodular goitre with a dominant nodule requiring permanent treatment due to the size, function, compressive symptoms, or those who cannot be operated for medical reasons, or who refuse surgery. A number of 30 patients will be treated with the minimally invasive technique based on percutaneous laser ablation (PLA).

Likewise, in accordance with Good Clinical Practice, the following groups of patients will be recruited:

- i) Patients who have compressive symptoms, nodules sized > 4 cm, or which cause a reduction in the tracheal and/or oesophageal lumen, will undergo surgical treatment (i1, $n = 10$). In the event of contraindications to surgery or refusal by patient, the laser ablation treatment will be proposed (i2, $n = 10$) versus follow-up (i3, $n = 10$).
- ii) Patients with nodules that measure between 2.5 and 4 cm that are symptomatic or with prolonged subclinical hyperthyroidism that do not cause any reduction in the tracheal or oesophageal lumen. Surgical treatment will be proposed (ii1 = 20) versus laser ablation (ii2, $n = 20$) versus follow-up (ii3, $n = 20$).

Participants assigned to the Percutaneous Laser Ablation (PLA) groups (i2, ii2) will be treated in an ultrasound-guided session.

In all patients, excepting those in the surgical group clinical, ultrasound and hormonal follow-ups will be carried out at 1, 3, 6 and 12 months.

Tests to be conducted and evaluation:

Specific statistical instruments will be used to comparatively evaluate the patients treated with APL versus the surgical and the follow-up groups in relation to:

- **The response to treatment:**
 - assessed by means of a $\geq 40\text{-}50\%$ reduction in the initial nodule volume and/or changes in the ultrasound characteristics to determine whether there are any predictive ultrasound characteristics of therapeutic effectiveness irrespective of the initial volume of the lesion;
 - a significant reduction in the compressive symptoms,
 - the maintaining of euthyroidism,
 - the changes in the patients' quality of life (Health questionnaire SF-36, post-op complications questionnaire, general wellbeing index questionnaire, pending thyroid questionnaire),
- **Major and minor intra- and peri-procedural complications**

for assessing the safety of the treatment,

- **Intervention and follow-up costs in order to compare them with the costs of conventional surgery in specific cases that allow for laser treatment,**
- **The cost-benefit ratio of the procedures.**

Expected results:

A significant reduction in the thyroid nodules, symptoms and the improvement in the quality of life while maintaining the euthyroid condition is expected for patients treated with percutaneous laser treatment. It is estimated that the intervention and the follow-up costs will be lower than those incurred with surgery in the cases treated through PLA. Depending on the results, another open, follow-up trial will be conducted to assess the long-term effectiveness of the treatment.

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ModiLite; a new reference for the Patients looking for Thyroid Nodule Benign solutions

Daria Bottacci

Welcome to
Daria Bottacci
Clinical Affair
and web master
<http://modilite.info>
website



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<http://modilite.info> Web master

What is ModiLite?

ModiLite is an outpatient minimally invasive ultrasound-guided treatment that uses the heat generated by a laser source to destroy portions of nodular tissue, causing a **progressive reduction in the thyroid nodule volume and subsequent disappearance of the compressive and aesthetic symptoms** in the neck.

Thanks to minimally invasive access with very thin needles inserted into optical fibres, **ModiLite** allows for destroying the neoplastic tissue, thus avoiding the trauma caused by surgical access (**absence of scars**), with evident advantages such as **no or much less post-op pain and complications**, an almost **immediate return to social life** and **life-long drug therapy is not required** as with surgical removal.

Why did you want to give a dedicated Name " ModiLite" to the Thyroid Laser Ablation Procedure?

The dedicate name Modilite is useful for Patients to identify the unique procedure of thyroid nodule laser ablation that we promote. The name ModiLite allows to differentiate our procedure from other laser-based techniques also based on the concept of thermal ablation. The ModiLite procedure uses a very thin needle (under 1mm) to introduce percutaneously fibre optics to deliver laser energy into the nodule and exploits unique laser and ultrasound technological innovation. Our innovations in ultrasound technology, for treatment monitoring, planning and verifying and in laser technology with a multisource laser with independent sources in activation and emission for an improved adaptability to each lesion, distinguishes ModiLite for easy performing, efficacy and safety.

Where can patients find information regarding ModiLite or receive information about a minimally invasive ultrasound-guided treatment that uses the heat generated by a laser source?

Visiting <http://modilite.info>. In this web page they can find information regarding What ModiLite is, Who can be treated in this way, The benefits of ModiLite, Treatment guide, Frequently asked questions, where to find Medical centres performing ModiLite closest to the Patient's Location, a request information form to ask more info about the treatment and much more.

Of course we are present also on Facebook at: <https://www.facebook.com/modilite> and on You tube https://www.youtube.com/watch?v=Y_sqm-TejBtE , <http://www.youtube.com/watch?v=09mM7bkevcE>

The <http://modilite.info> is a further tool available for the patient to have useful information about the ModiLite procedure. The main target is to make easy contacts between the patients and the centres which perform Minimally invasive Thyroid Therapy. It can be a good partner to Endocrinologist Physicians and to several Echo laser Members.

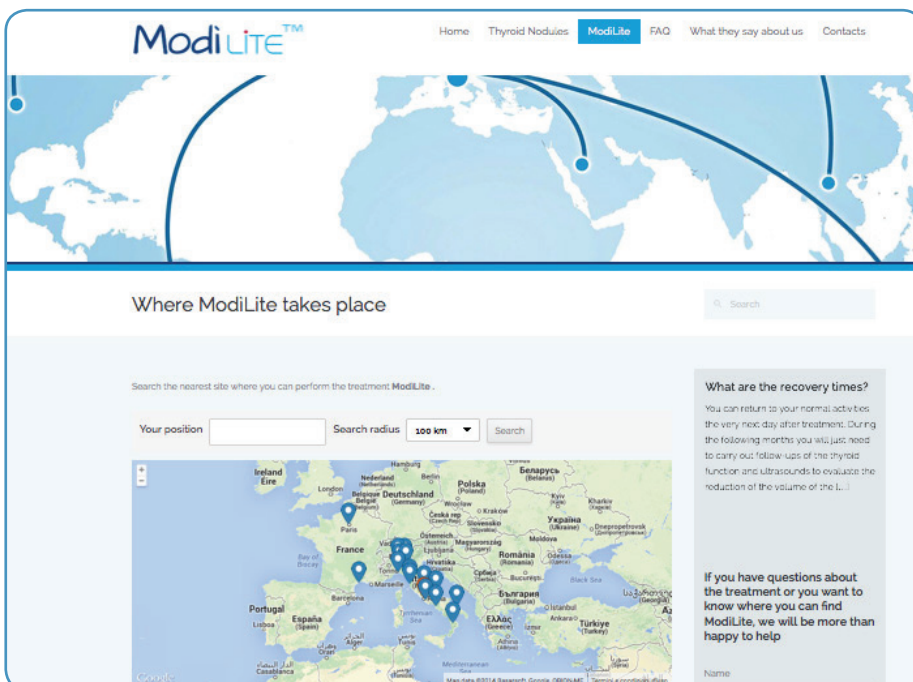
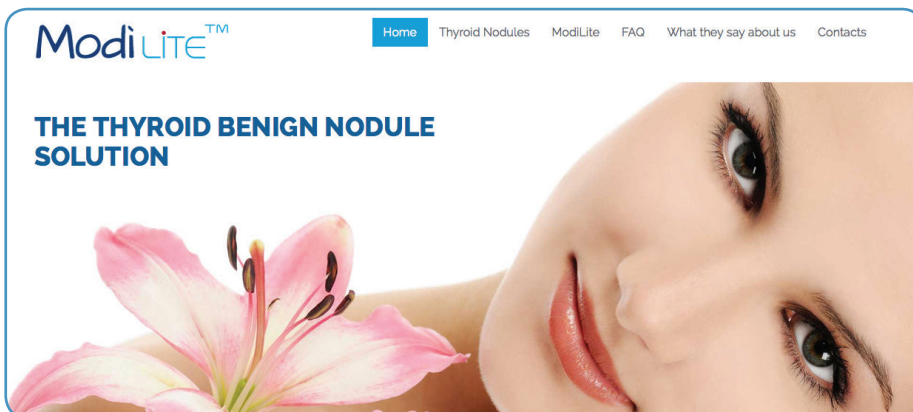
Your contributions are welcome!

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