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Minimally invasive procedures for symptomatic thyroid lesions

A nonsurgical approach for changing the natural history of growing benign thyroid nodules

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Background

Thyroid nodules are a common clinical problem that carries a low (about 4-6%) risk of malignancy. Their current management with TSH determination, thyroid sonography (US) and US-guided fine needle aspiration biopsy (FNA) provides a reliable identification of benign nodules. The majority of these do not need any treatment after exclusion of malignancy or abnormal thyroid function[1-2].

A minority of benign nodules (probably about 10%) shows a progressive growth that may induce local symptoms or concern. Routine use of T4 suppressive therapy is presently not recommended because results in a clinically significant nodule shrinkage only in a minority of patients and is potentially associated with adverse side effects[1-2]. On the long-term, even in the absence of suspicious US or cytological findings, discomfort or anxiety may become ill-tolerated and are frequently followed by surgical consultation.

Surgery is the traditional therapeutic option for benign thyroid nodules which gradually grow or become symptomatic[1-2]. However, the cost of thyroid surgery, the risk of possible complications and the potential impairment of the quality of life remain non negligible problems[3]. On these basis, various minimally-invasive procedures (MIT) for an office-based treatment of growing nodules with minimal damage to cervical tissues have been proposed during the last two decades[4].

Approach to Minimally-invasive procedures

Relapsing benign thyroid cysts are rapidly and inexpensively managed with US-guided ethanol injection (PEIT), which should be considered their first- line treatment[2,4].

PEIT is a simple and safe procedure and requires only the availability of an US machine and sterile 95% ethanol vials. Operators with sufficient experience in US-guided FNA and thyroid cysts drainage require a short period (not exceeding few days) of practice in this procedure.

Thermal ablation requires LAT devices that employ disposable kits with an average cost of 500 euros for treatment[4]. These technologies are mostly available in hospital-based thyroid centers and require a proper training. The procedure is rather simple and easily monitored, but its inappropriate use could potentially damage vital cervical structures[5-6]. LAT requires the correct positioning of one or two guiding needles within the target lesion and a careful US monitoring during the following 5-10 minutes of laser firing[5-6]. Operators with experience in US-guided FNA require a dedicated period of training (about one week) in a specialized center and, thereafter, should start their activity under the initial supervision of an experienced tutor.

Techniques of treatment

The main advantage of MIT over traditional surgical resection is the capacity to destroy only a small volume of normal tissue surrounding the target lesion while completely preserving the organ function[6]. Continuous imaging allows the accurate placement of applicators and the monitoring of the coagulation zone during treatment. US, CT, and MRI may all be employed, but US is the most accessible and practical imaging tool for real-time monitoring of MIT.

Percutaneous ethanol Injection. After local anaesthesia, a 21- to 23-gauge needle is placed under US guidance into the target lesion. In thyroid cysts, after the drainage of the fluid component, 95% ethanol is slowly injected into the cavity and then the needle is withdrawn with or without alcohol aspiration. Cyst treatment is rapid, inexpensive, nearly painless and quite safe. Chemical injury induces protein coagulation and small vessel thrombosis which are followed by progressive fibrosis and shrinkage. PEIT is a rapid outpatient procedure in cysts up

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to 3 cm in diameter. Multiple sessions are usually needed for the complete ablation of large or multiloculated complex lesions.

Laser ablation. Thermal techniques ablate tissues by increasing or decreasing its temperature so as to cause an irreversible cell damage. When tissue temperature raises to between 60 and 100°C, coagulation irreversibly damages cell proteins and nuclear DNA. Temperatures over 100°C are followed by tissue carbonization that may hamper the optimal diffusion of heat within the target lesion[4].

Laser light is transmitted from its source (mostly Nd: YAG or diode lasers) to the patient by means of thin, flexible, optical fibers. LAT is performed inserting under US guidance, after a mild local anesthesia, from one to two 21-gauge spinal needle(s) into the target lesion. After the assessment of the correct positioning of the needle(s), a 300 µm-diameter plane-cut quartz optical fiber is introduced through the sheath of each needle until the fiber tip is placed in direct contact with the tissue. Illuminations performed with an output power from 2 to 5 watts for a time from 5 to 10 minutes cause a tissue damage characterized by a small zone of cavitation encircled by a broad area of coagulative necrosis. A spherical volume of coagulative necrosis up to 2 cm in diameter can be produced from a single fiber. For larger volumes of necrosis, multiple optical fibers may be arrayed at 1.5-cm spacing throughout the target lesion or cooled-tip diffuser fibers may be used[4].

Radiofrequency, microwaves, high-intensity focused ultrasound and transarterial embolization are promising techniques but should still be considered as less simple, time-consuming and cost-effective procedures for thyroid lesions[4,7].

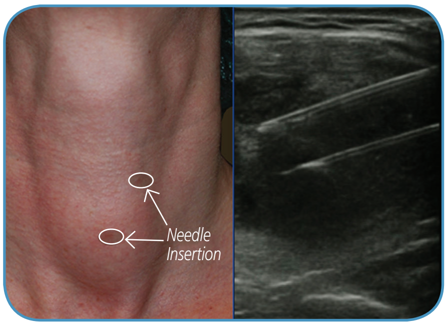
Conclusions

Relapsing thyroid cysts and complex nodules should be currently managed with aspiration followed by PEIT as their first line treatment.

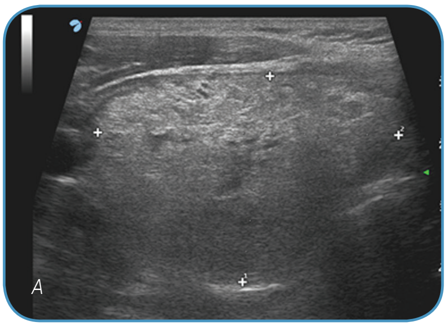
In solid nonfunctioning symptomatic thyroid nodules LAT usually results, in a single session, more than 50% volume decrease and improvement of pressure symptoms[6-8].

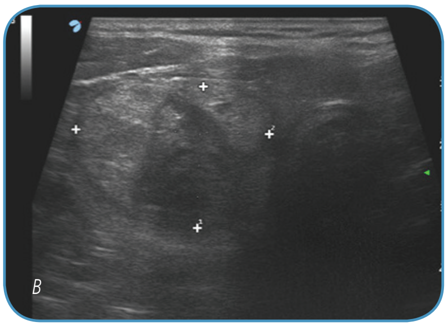
Large hyperfunctioning thyroid nodules remain best treated with radioactive iodine, but a preliminary treatment with LAT significantly decreases the total activity of radioiodine needed for their effective ablation[4].

Head to head prospective studies of thermal ablation versus surgery comparing long-term efficacy, side-effects and overall expense are needed to confirm the role of MIT in every day practice and their possible application to the non surgical management of cervical recurrences of thyroid cancer[9-13].



Multifibre approach (Two fibres) and aesthetic result of the needle insertion after treatments





Solid benign thyroid nodule a) before treatment nodule is an iso-echoic tissue with a 45 ml volume, with small anechoic lesion and presence of halo signs; b) US image 12 months after PLA, shows a 74% volume nodule reduction.

Abbreviations

AFTN: Autonomously functioning nodules; **CT**: Computerized tomography; **FNA**: Fine-needle aspiration biopsy; **131I**: Radioiodine; **LAT**: Laser ablation treatment; **mm**: millimeter; **MRI**: Magnetic resonance imaging; **MIT**: Minimally-invasive treatment; **PEIT**: Percutaneous ethanol Injection treatment; **RFA**: Radiofrequency Ablation; **US**: Ultrasound.

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Cooled Thermal Ablations Devices; Physical considerations

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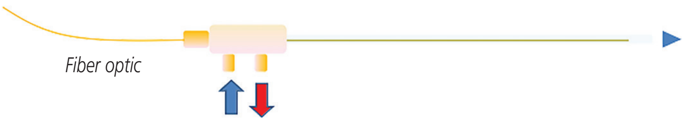
Nowadays thermal ablation of tumors inside human body can be done by means of different technologies: laser, microwave, radiofrequency, cryotherapy, HIFU (High Intensity Focalized Ultrasound); each one have advantages and disadvantages.

A common feature of the three technologies microwave, laser and radiofrequency (RF) is the recent development of electrodes or needles, i.e. the applicators, with a cooling system in the active portion of the shaft from which energy is transmitted to the tissues to be treated. The thermal treatment causes the denaturation of proteins which is followed by necrosis.

The cooling effect is performed by means of a fluid circulation inside the applicator able to remove from it a part of the heat in ordert to maintain its temperature at a level that will not create undesirable effects during the treatment.

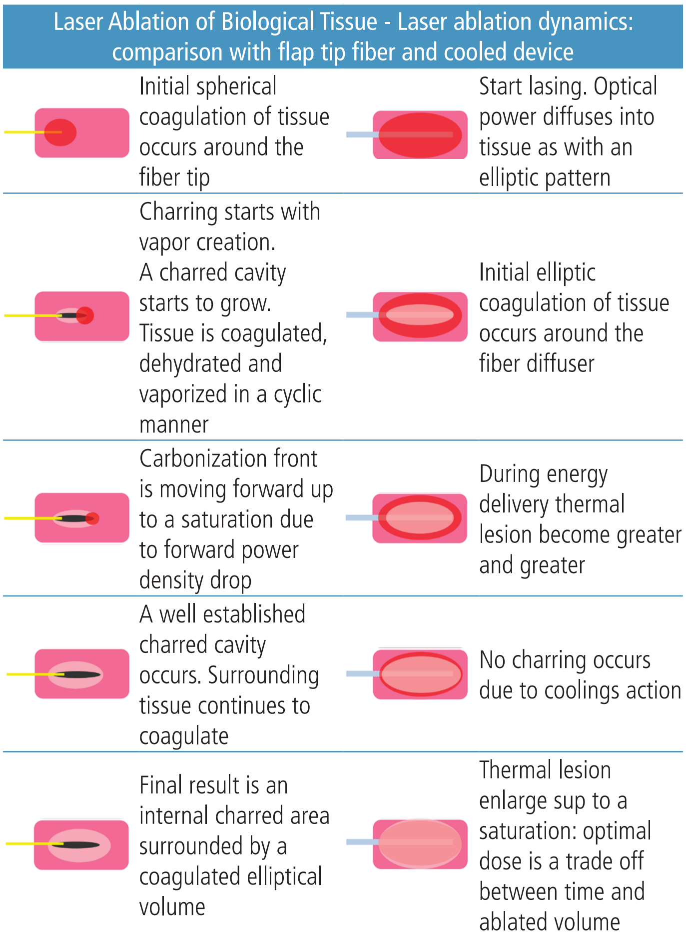


The undesirable effects are of two types and are of different forms according to the technology used (microwave, laser or RF). Common to all is the generation of carbonization of biological tissue around the issuer portion of the applicator.

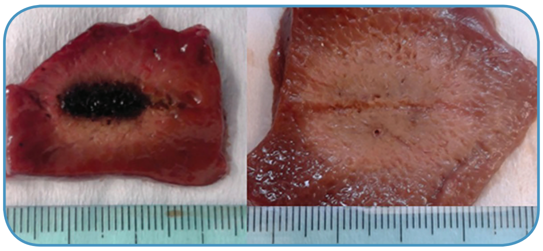
Carbonization happens because the delivered energy has the maximum density near the applicator, whereas the energy is reduced on farer tissue portion due to the absorption of the near zones. Moreover the density is reduced because it is distributed on bigger and bigger surfaces as the distance from the applicator increase. You can think about marble or granite thresholds of shopping centers doors: they are more consumed compared with the rest of the inner floor even if they are built with the same material, because once they have entered, people go in different directions, therefore the density of passing people changes and the number of steps per surface unit on the floor is reduced as well as the consumption of its constituting material.

Carbonization in the first zones derives from the maximum accumulation of energy causing the maximum rise in temperature, consequently the vaporization of all intra and inter cellular fluids, the destruction of molecules with release of hydrogen and oxygen atoms and the constitution of conglomerates almost totally made of carbon atoms; at a higher temperature combustions would be caused by the union of carbon and oxygen atoms that could be present in the environment.

Holding low temperature in the tissue in contact with the cooled applicator avoids the temperature rise in treated tissues and therefore the carbonization process.



Avoiding carbonization is necessary since it is the main cause of limitation of the volume of thermal damage (necrosis) that has to be caused in tissues.



Flat tip vs cooled device

The quantity of energy removed from the cooling fluid circulating inside the applicator is taken away from the energy delivered by the generator device and therefore reduces the quantity provided to tissues.

The reduction of energy provided to tissues due to applicator cooling can be compensated either by increasing the length of treatment at fixed power or appropriately increasing the power of the generator.

Another target of cooling is to keep low electrodes temperature, within control limits. In particular for some technologies, i.e. microwave and radiofrequency, the cooling through fluid circulation allows to obtain the limitation of temperature of the applicator's metal surfaces both in the external and internal part.

The heating of the internal and external surfaces of the applicator electrode is due to the heat produced by strong electric currents running through it causing Joule effect. This is mostly important for microwaves, because of the higher frequency compared with radiofrequency that for skin effect reduces the thickness of the surfaces metal in which the currents run.

Electrodes, if not cooled, could create skin burns around the entry hole and along the needle's way up to the lesion to be treated.

Thanks to laser technology, the energy is transmitted to the tissues to be treated by means of the light guided in the optical fiber inside the introducer needle. There are no electric currents involved and therefore no metal heating caused by Joule effect. There can be burns, even though little, on the skin if the operator makes the error of not hanging out, as usual, the fiber optic from the needle tip to freely irradiate the tissues with the light; otherwise the final part of the needle tends to increase the temperature of the metal by absorption heating the needle shaft up to the introduction hole by heat conduction. Needles containing optical fiber inside for this specific use are provided with fiber stop that automatically assure the exit of the right quantity of the fiber tip (5 or 10 mm) from the terminal allowing to provide light energy only in the adjacent tissue to be treated.

The ETA Annual Meeting offers a unique opportunity for Echolaser Club to meet and increase internal discussion about **minimally invasive treatment of benign thyroid nodules**

Save the date Saturday 6th of September Echolaser Club Social Evening

All the Echolaser Members present in at ETA congress are invite to partecipate.

Please contact **anouk.pluijmeekers@esaote.nl** to confirm your partecipations and to receive the invitation for the Social Evening.

Looking forward to see you in Santiago de Compostela.

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