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ECHO LASER News

# Minimally invasive treatments for Metastatic Lymph Nodes in the Neck from Papillary thyroid carcinoma

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## Background

Thyroid cancer represents the most common cancer of the endocrine system. In 2014, 62,980 new cases and 1,890 deaths are estimated to occur in the United Sates. Thyroid cancer occurs more frequently in women than in men, and represents 5% of estimated new cancer in women. Papillary carcinoma is the most frequent among thyroid cancers subtypes, accounting for about 85% of all thyroid cancers[1-3]. The most common clinical presentation of thyroid cancer is a thyroid nodule, either solitary or within a multinodular goiter. Thyroid ultrasound is now widely available and affordable and allows to identify and follow thyroid nodules, assess neck lymph nodes status, and guide fine needle aspiration for precise diagnosis.

Once diagnosed, the treatment of papillary thyroid carcinoma is based on total thyroidectomy, generally associated with central neck dissection. In case disease is present in the lateral neck compartment pre-operatively, lateral neck dissection is generally performed at the time of thyroidectomy, while the role of prophylactic neck dissection is still debated[4–7]. Following surgery, radioidine ablation is often performed in order to destroy any remaining normal thyroid tissue and any occult microcarcinoma [8,9].

Unfortunately, after treatment cervical nodal recurrence may occur in up to 30% of patients[10,11]. Thus, a strict follow-up is crucial after surgery in patients treated for papillary thyroid carcinoma. Currently, follow-up is mainly based on serial serum thyroglobulin (Tg) measurements and neck US to search for local recurrence or development of cervical lymph nodes metastases[4,5,12]. Radioiodine 131 scan may be helpful in identifying residual disease, and, in case of recurrence, radio-iodine ablation can be performed. However, some well differentiates tumours may lose their capability to uptake the radioiodine. In these cases, 18F-fluorodeoxyglucose positron emission tomography (18FDG-PET) may be useful to detect recurrent or metastatic lesions[13,14].

In cases of recurrence, repeating surgery may be challenging even for experienced surgeons, and related with increased morbidity rates[4,6,11]. Moreover, it may not be even treatable with radioiodine ablation, as tumours may have lost their ability to uptake radioiodine.

Finding less invasive alternatives than repeat surgery for metachronous metastases may be extremely helpful in order to avoid morbidity related to repeated neck dissections. Percutaneous treatments are minimally invasive, can be performed without general anaesthesia, require shorter hospitalization and are generally less expensive than open surgery. In addition, percutaneous treatments can be performed several times without increased technical difficulties due to the previous treatments. With percutaneous treatments, patients avoid the morbidity and the recovery time related to neck open surgery, and can resume their normal activity from the day after the procedure. Several different techniques are nowadays available for percutaneous treatments, and some of them have been reported in the treatment of neck diseases.

## Percutaneous Ethanol Injection

**PEI** was first introduced in 1985 for the treatment of hyperparathyroidism, and then was employed to treat both hyperfunctioning nodules and benign cold and cystic nodules of the thyroid gland[15–17]. The procedure consists in the injection of 95% ethanol through a 21-23-gauge needle placed under US guidance into the metastatic lymph node. Ethanol causes coagulation necrosis because of cytoplasm dehydration and protein denaturation and small vessel thrombosis. Later, progressive fibrosis and shrinkage occur. Hay et al.[18] used this technique for the treatment of 29 lymph node metastases in 14 patients and achieved a mean volume reduction from 492 $mm^3$ to 20 $mm^3$ at 2 years. Heilo et. al[19] reported a volumetric reduction in

93% of 109 lymph nodes treated with **PEI**, with a complete response to **PEI** treatment in 84% of the treated cases. This technique is fast, quite easy and inexpensive. However, generally several treatments are necessary to achieve a complete treatment, extent and morphology of necrosis are not well predictable and reproducible, and side effects may occur (i.e. pain, surrounding tissues sclerosis, and nerve damages) , mainly because of undesired leakage of ethanol during the procedure. Due to these technical limitations, this therapy is almost abandoned for solid thyroid lesions.

## Radiofrequency Ablation

**RFA** was the first technique used for image-guided thermal ablation. Traditionally used for liver, **RFA** is applied through an electrode to induce high-temperature cytotoxic heating in target tumors. The patient is part of a closed-loop circuit (made by electrode, power generator, and grounding pads). That creates an alternated electric field inside the patient. As biological tissues are poor electric conductors, ionic friction takes place and leads to heat generation. High temperature implies tissue dehydration and water vaporization, thus leading to coagulative necrosis.

Some authors used **RFA** for treatment of metastatic lymph nodes in the neck, using electrodes of small caliber (17-18 G) and short exposed tip (0.5-1.0 cm). Dupuy et al.[20] reported on the use of radiofrequency ablation for the treatment of 8 patients with regional recurrence from well-differentiated thyroid malignancy. They used a 17-gauge, internally cooled electrode and obtained good local control of treated lymph nodes. One patient in their series suffered vocal cord paralysis, and one developed a skin burn related to the treatment.

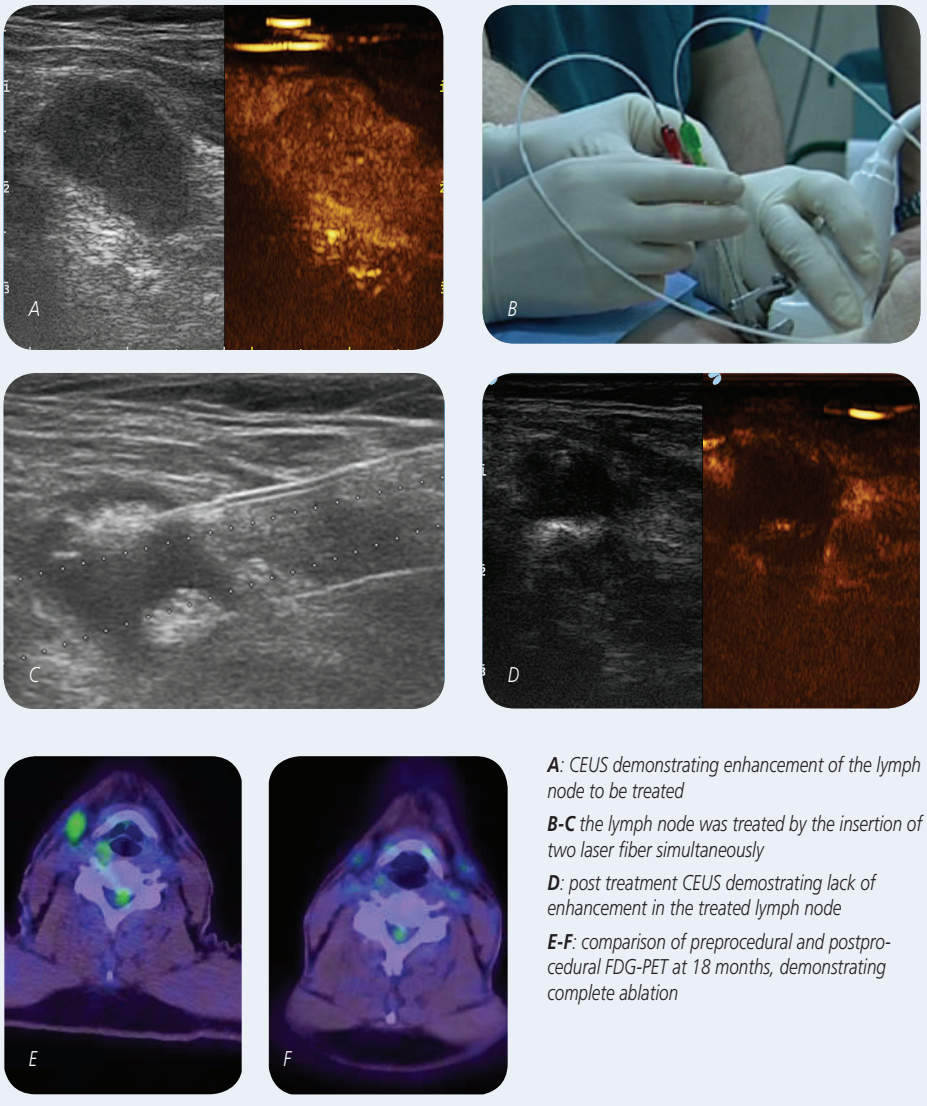
Guenette et al.[21] achieved a complete local control in 21 lymph nodes treated with this technique in a mean follow-up of 61.3 months, with one case of permanent vocal cord paralysis. Baek and colleagues[22] treated 12 lymph node metastases in 10 patients with **RFA**, and reported a volumetric reduction from 55.5 $mm^3$ to 5.7 $mm^3$ and a reduction of thyroglobulin serum levels below the limit in 7/10 patients with a follow-up of more than three years. One case of vocal cord paralysis occurred.

## Percutaneous Laser Ablation

Percutaneous laser ablation (**PLA**) has been successfully used for liver tumor treatment[23] and in the neck for the treatment of thyroid nodules less invasively than surgery[24–26]. The major advantage of laser over other ablative techniques is its ability of inducing a predictable and well-defined area of necrosis, making this technique theoretically of particular value in small tumors close to important or thermally-sensitive structures, including metastatic lymph nodes in the neck.

We started to use **PLA** for the treatment of metastatic lymph nodes from papillary thyroid carcinomas in September 2010. We perform this procedure in the ultrasound interventional room, using local anesthesia and bland sedation only if needed. Before treatment, each lymph node is carefully evaluated by ultrasound and contrast-enhanced ultrasound (CEUS) to document baseline nodal perfusion. The patient is placed on an operation table in supine position with hyper-extended neck. We use a commercially available ultrasound system (EchoLaser X4©, Esaote, Genoa, Italy), equipped with dedicated linear transducer operating at 13-4 MHz and with needle-guide attachment with adjustable angle selection. Once the best path to the target is identified, skin and subcutaneous tissues are anesthetized with a combination of 2 ml of 2% lidocaine and 3 ml of ropivacaine (Naropine©, Fresenius Kabi, USA). Next,

*Patient 61-year old female patient, with a 1.8 cm metacronous metastasis at the level of one right cervical lymph node. The patient previously underwent thyroidectomy and lymph node dissection.*




***A**: CEUS demonstrating enhancement of the lymph node to be treated*

***B-C** the lymph node was treated by the insertion of two laser fiber simultaneously*

***D**: post treatment CEUS demostrating lack of enhancement in the treated lymph node*

***E-F**: comparison of preprocedural and postprocedural FDG-PET at 18 months, demonstrating complete ablation*

the number of guide needles to be inserted (usually one or two) is established based upon lymph node size and shape as well as calculation of the best needle path to achieve optimal ablation with the fewest needle insertions. If possible, we try to insert laser fiber along the major axis of the lymph node to permit subsequent pullback for multiple sequential applications in case of elongated lymph nodes. In some cases, to better identify the lymph node to be treated and the best approach to it, pre-acquired images from other modalities (such as computed tomography or 18FDG-PET) can be fused in real-time with US images using a dedicated software (Virtual Navigator, Esaote, Genoa, Italy). Then, one or two 21-gauge needles are inserted into the target lymph node under real-time ultrasound guidance. Once proper needle positioning is documented, a 300 µm quartz optic fiber with optically flat end is inserted into the needle and advanced up to its tip. The needle is then withdrawn to expose the fiber by at least 5 mm. The optic fibers are then connected to the laser source, a continuous-wave Nd-YAG laser operating at 1.064 mm (EchoLaser X4©, Esaote, Genoa, Italy).

Each treatment is performed using 3 or 4 watts power, changing the application time case by case according to target size, shape and the feedback from real-time US monitoring to maintain the total energy applied between 1,200 and 4,200 joules. At the end of the ablation session (which can include multiple **PLA** applications), CEUS is performed to assess the lack of enhancement in the treated target. In case of incomplete ablation, a new optic fiber is inserted at the level of the untreated portion and subsequent ablation is performed. We recently reported our preliminary experience using this technique in 24 metastatic lymph nodes in 15 patients[27]. All patients were unsuitable or refused surgery, were not treatable with radioiodine ablation, and had PET/CT positive lymph nodes. **PLA** was always feasible in our series, and technical success was achieved in all patients. At the 12-month follow-up, local control was achieved in 71.4% patients and 80% of treated lymph nodes were negative at PET/CT and CEUS, with no major complications.

## Conclusions:

To find less invasive alternatives to surgical resection may be extremely helpful for patients with metacronuos metastases from papillary thyroid carcinoma in order to avoid the morbidity related to repeated neck dissections. Percutaneous image guided treatments represent the ideal alternative treatment, as they are minimally invasive, can be performed without general anaesthesia, require shorter hospitalization time and are generally less expensive than open surgery. Moreover, percutaneous treatments can be performed several times without increased technical difficulties due to the previous treatments. Among all different available techniques, **PLA** has several theoretical advantages particularly for treatment in the neck. First, a very small needle can be used to reach the target, thus theoretically reducing problems in such a complex region, were often lymph nodes are close to important and sensitive structure such as vessels and nerves.

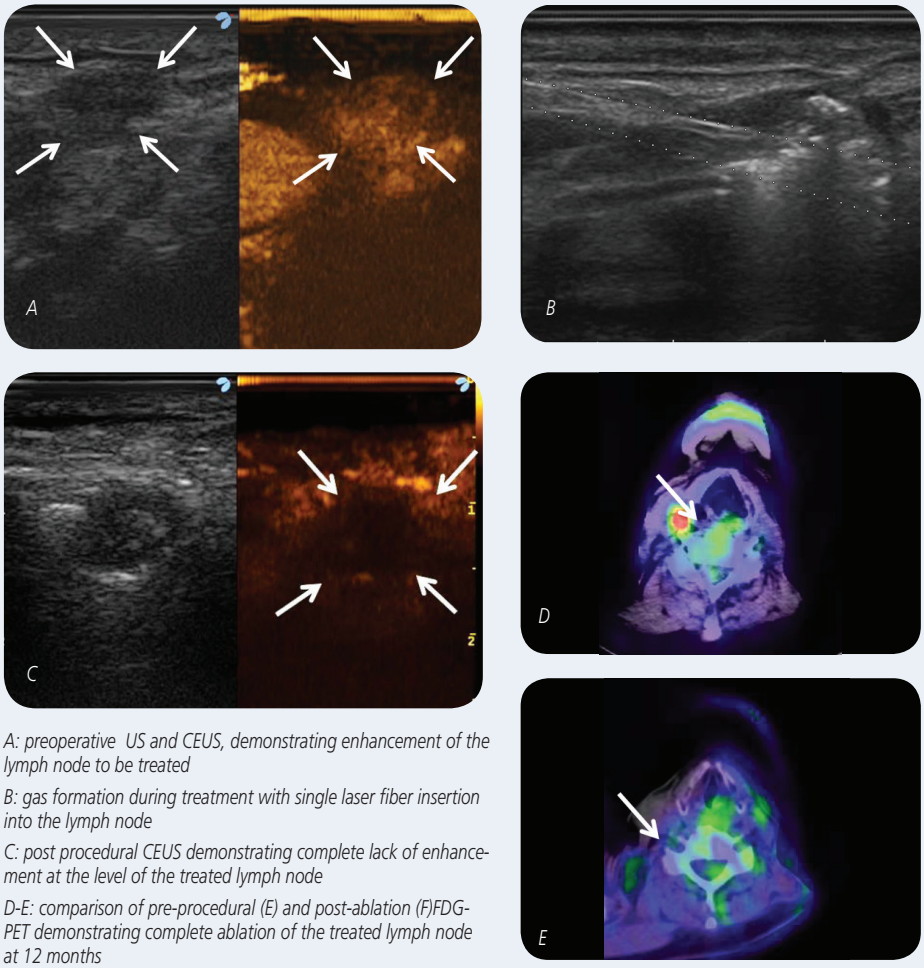
Moreover, thermal energy is deployed very precisely and in a high predictable way with laser, and small ablation volumes can be more precisely obtained, thus theoretically minimizing risks of burning undesired structures such as nerves or skin. Furthermore, if larger ablations are required, several different needles can be placed simultaneously using the same dedicated needle guidance.

One of the major advantages of **PLA** is that this technique can be repeated several times without increased technical difficulty due to previous treatments, as happens for surgical resection.

Due to this fact, and to the good results in terms of local control rate, we envision a scenario where low risk patients could be treated with thyroidectomy alone and with **PLA** in case of development of metachronous lymph node metastases, with the advantage of reducing the number of unnecessary preventive dissections and of minimizing the morbidity of a second surgical operation.

In conclusion, **PLA** likely represents a new option in the treatment of metastatic lymph node in the neck from papillary thyroid carcinoma. Such a technique appears to be feasible, safe, and effective and may allow to completely treat or to avoid unnecessary surgery in a high amount of patients.

*Patient 51-year old male patient previously treated with thyroidectomy, radioiodine ablation e repeated lateral neck dissection who developed a metacronuos , 1.5 cm, right nodal metastasis, and was treated with percutaneous laser ablation*




*A: preoperative US and CEUS, demonstrating enhancement of the lymph node to be treated*

*B: gas formation during treatment with single laser fiber insertion into the lymph node*

*C: post procedural CEUS demonstrating complete lack of enhancement at the level of the treated lymph node*

*D-E: comparison of pre-procedural (E) and post-ablation (F)FDG-PET demonstrating complete ablation of the treated lymph node at 12 months*

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# Welcome to Prof Hu Bing

**Prof Hu Bing**
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## You have worked for many years in Urology department before you became a specialist in ultrasound medicine, so in term of your experience, why it is important and useful Echolaser in prostate ablation treatment?

Thermal therapy as an important tool has been widely used in lesion ablation, such as RF and MW etc. in different applications.

When it comes to prostate disease treatment, we faced the difficulties coming from RF or MW because of its higher energy hard to control over, too bigger size of the needles dangerous to the critical structures nearby.

However, I tried Echolaser from Esaote Italy, it has demonstrated many strengths, for instance, the size of ablation is well controlled, the border of treatment volume is clear-cut and moreover, to treat a lesion inside just takes few minutes with fairly low energy emitted.

Since February 2012,we have preliminarily treated some cases of patients with prostate cancer in our group and we obtained much satisfactory effect.

## Did you try laser treatment method to other applications, for example liver lesion or some masses of kidney?

Yes for sure. Because when I visited a site in Rome where Echolaser is frequently utilized in liver lesions and thyroid nodules,

I discovered the outstanding effect that with 4 fibers the ablation size could reach more than 4 CM with a called multiple-fiber technique applied to liver.

After coming back to China, I tried and I confirmed such result and usefulness, wich could be comparative to RF I used as a routine tool before. Apart from that, we tried it also for kidney lesions especially when the real unit is needed to be overwhelmingly preserved.

## My Tips & Tricks for treatment of Localized Prostate Cancer with Ultrasound guided Laser Ablation:Clinical Cases

As the common tumors in men for prostate cancer, the incidence is rising at present in China. Data shows that Shanghai witnessed 9th of malignant tumors in the prostate cancer in men.

In recent years, the literature reported the ablation of advanced prostate cancer with long-time treatment by low-power laser has achieved a certain effect. However, the efficacy of treatment for localized prostate cancer with high-power laser was rarely elaborated.

Since February 2012 for laser treatment of 3 cases with prostate cancer in our group, we obtained more satisfactory effect. The report is as follows.

**Clinical Data**:

Group of 3 cases, the age of 60~75 years old. One case has only increased nocturia, one case hematuria, and the left, no clinical symptoms or abnormal results with laboratory test. Two cases with diabetes mellitus, one case had TURP surgery and one with one touchable nodule in hard prostate. Preoperative ultrasound examination indicates prostate cancer. Two PCa prompted through routine MRI. Preoperative PSA measurements in 10~15ng/ml, pathology confirmed for prostate cancer via prostate biopsy, of which 1 tiny cancer, one case Gleason score 3+3 and the left, Gleason score point of 3+3 with peripheral nerve invasion. Three cases had no seminal vesicle invasion, no bone and lung metastasis.

**Instrument used**:

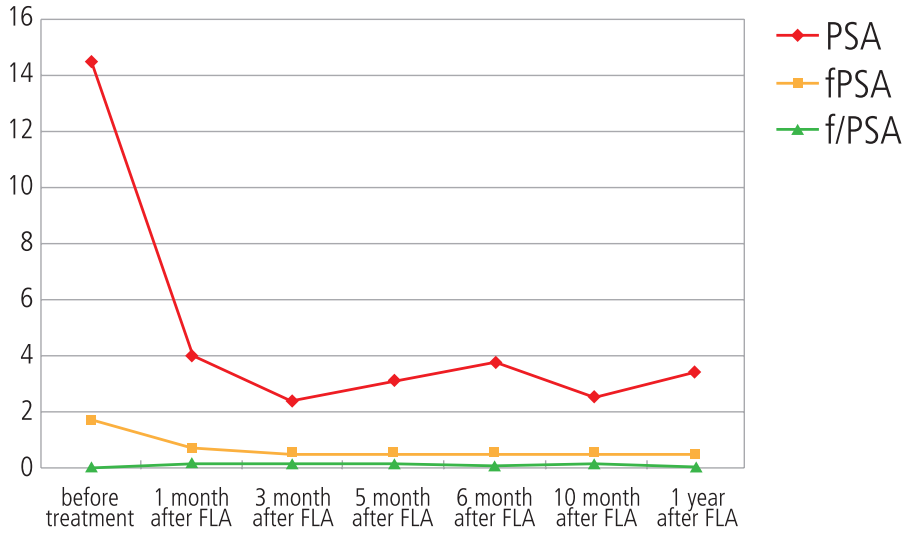
Echolaser Mylab Twice and TRT33 probes (Transrectal bi-plane cavity probe) with Assisted positioning system: three dimensional planning system, fixing bracket .

**Methods**:

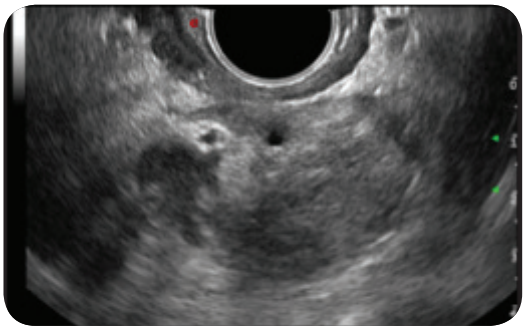
Positioning patients with lithotomy, intravenous anesthesia, monitoring bedside vital signs, preoperative detaining three cavity catheter, rectal probe with fixed supports as backup.

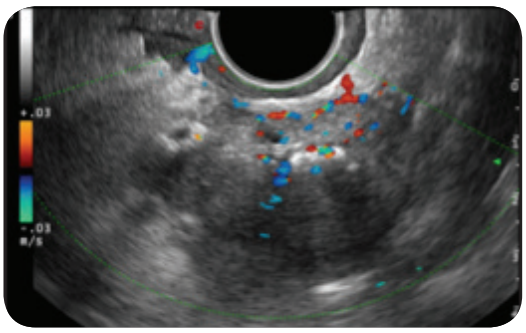
After sterilization with towels in perinea, patients with rectal probe into the rectum, observe closely echoes for the prostate size, distribution and determining the urethra location as well.

According to the regional treatment plan of laser ablation, induce fibers in advance through a template into the prostate; adjust its spatial location and then perform ablation. Treat in several procedures and after 15 minutes, by contrast-enhanced ultrasound, to evaluate the range of laser ablation. If there is some areas not well treated, once again. Bladder irrigation method is applied in order to protect the urethra.




| | PSA (ng/ml) | Volume (ml) | PSAD |
|---|---|---|---|
| Before treatment | 14.488 | 42.68 | 0.339 |
| 1months after FLA | 62.714 | 47.62 | 1.317 |
| 3 months after FLA | 4.02 | 40.77 | 0.099 |
| 5months after FLA | 3.108 | 34.40 | 0.090 |
| 7 months after FLA | 3.833 | 37.91 | 0.101 |
| 1 year after FLA | 3.476 | 34.34 | 0.101 |





Hypoechoic area in the right lobe, with no vascularity, 1 month after **FLA**

**Results:**

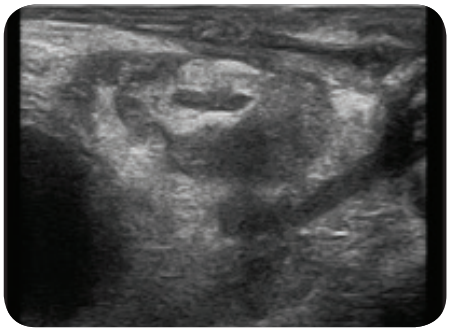
2-3 days after to removing catheter, only 1 case urinating incomplete after removal of catheter tube (residual urine 350ml), catheterization again and after the treatment with Proscar, the patient is able to recover. The remaining two can urinate on their own. Two cases after 1-2 months, PSA dropped down to be normal (2 ng/ml), 1 case did not get down to normality, but compared with preoperative result, PSA has reduced considerably. There is no contrast enhancement with CEUS in the ablation areas. MRI shows no enhancement in the center of ablation areas while peripheral strengthened.

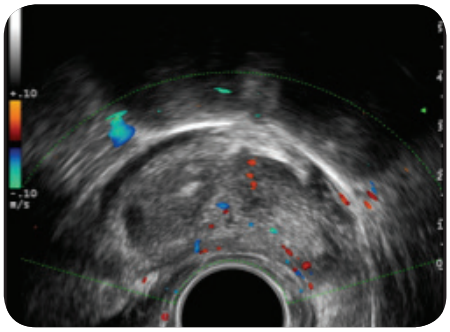
**Conclusions:**

Laser ablation method in the treatment of localized prostate cancer has been initially established, and adaptive ablation for prostate cancers is under track.

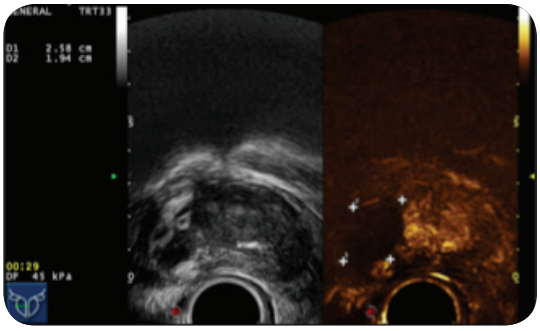
Nevertheless, its long term-efficacy remains to be evaluated in order to address such issues further.

Above all, we believe this kind of treatment technology will become an important way to deal with prostate cancer.





In the right peripheral zone with no obvious vascularity, 3 months after **FLA**



No enhancement in ablation area in right lobe

**Echolaser news are available at**
www.elesta-echolaser.com/it/rassegna-stampa/

**Echolaser Club'contacts**
Echolaserclub@esaote.com


## 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 welcome to partecipate.

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

## Looking forward to see you in Santiago de Compostela.

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