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1. **B. Lang et al.** A prospective study on the efficacy of single high intensity focused ultrasound treatment of patients with benign symptomatic thyroid nodule

2. **R. Kovatcheva et al.** The effect of different treatment regimen with US-guided HIFU on thyroid nodule volume

Treatment of breast fibroadenoma with echotherapy

THERACLION

Abstracts of relevant publications

Long-term efficacy of ultrasound-guided high-intensity focused ultrasound treatment of breast fibroadenoma

R. Kovatcheva, K. Zaletel, J. Vlahov, and J. Stoinov; Journal of Therapeutic Ultrasound; 2017

Background

To assess the long term efficacy and tolerability of one or two ultrasound (US)-guided high-intensity focused ultrasound (HIFU) treatment in patients with breast fibroadenoma (FA).

Methods

Twenty patients with 26 FA were selected for US-guided HIFU. The therapy was performed in one or two sessions. FA volume was assessed before and followed up to 24 months after the last HIFU. After each treatment, adverse events were evaluated.

Results

In 19/26 FA (73.1%) one HIFU was performed (group 1), whereas 7/26 FA (26.9%) received second HIFU (group 2) 6-9 months (median, 7 months) after the first session. In group 1 and 2, FA volume decreased significantly at 1-month ($p < 0.001$) and 3-month follow-up ($p = 0.005$), respectively, and continued to reduce until 24-month follow-up ($p < 0.001$ and $p = 0.003$, respectively). At 24 months, mean volume reduction was 77.32% in group 1 and 90.47% in group 2 ($p = 0.025$). Mild subcutaneous edema was observed in 4 patients and skin erythema in 3 patients.

Conclusions

US-guided HIFU represents a promising non-invasive method with sustainable FA volume reduction and patient's tolerability. Although one treatment is highly efficient, the volume reduction can be increased with second treatment.

Find the article online:

https://jtultrasound.biomedcentral.com/articles/10.1186/s40349-017-0083-1

High intensity focused ultrasound in the treatment of breast fibroadenomata: results of the HIFU-F trial

MC. Peek, M. Ahmed, J. Scudder, R. Baker, SE. Pinder, M. Douek; HIFU-F Trialists' Group.
Int J Hyperthermia. 2016 Sep 7:1-8.

Objectives

Breast fibroadenomata (FAD) are the most common breast lumps in women. High intensity focused ultrasound (HIFU) is a non-invasive ablative technique that can be used to treat FAD but is associated with prolonged treatment times. In the HIFU-F trial, we evaluated the change in volume over time with circumferential HIFU treatment of FAD and compared this to no treatment.

Methods

Patients ≥18 years, diagnosed with symptomatic, palpable FAD, visible on ultrasound (US) were recruited. Twenty patients were treated using US-guided HIFU under local anaesthesia. Another 20 participants underwent an US 6 months after diagnosis. Outcome measures included: reduction in treatment time compared to whole lesion ablation; feasibility to achieve a 50% reduction in volume after 6 months; decrease in volume compared to a control group and reduction in symptoms.

Results

Circumferential ablation reduced the mean treatment time by 37.5% (SD 20.1%) compared to whole lesion ablation. US demonstrated a significant mean reduction in FAD volume of 43.5% (SD 38.8%; $p = 0.016$, paired t-test) in the HIFU group compared to 4.6% (SD 46.0%; $p = 0.530$) in the control group after 6 months. This mean reduction in FAD volume between the two groups was significant in favour of the HIFU group ($p = 0.002$, grouped t-test). Pre-treatment pain completely resolved in 6 out of 8 patients 6 months post-treatment.

Conclusion

Circumferential HIFU ablation of FAD is feasible, with a significant reduction in pain and volume compared to control participants. It provides a simple, non-invasive, outpatient-based alternative to surgical excision for FAD.

Find the article online:

http://www.tandfonline.com/doi/abs/10.1080/02656736.2016.1212278?journalCode=ihyt20

Thermosurgical Ablation of Breast Fibroadenoma First experiences with a HIFU system

M. Hahn, B. Böer, M. Marx, E. Oberlechner, R. Fugunt, I. Gruber, G. Helms, C. Röhm, S. Brucker

Senologie; 2016

Breast fibroadenoma (FA) is the most commonly reported breast tumour in adolescents and young women. The traditional management option is surgical excision. Recently, minimally invasive options have been developed including cryotherapy, ultrasound (US)-guided vacuum-assisted biopsy, and thermoablation methods that include radiofrequency ablation and laser ablation. US-guided high-intensity focused US (HIFU) is a new method for treating FA. Currently, the Center for Women‘s Health at the University Hospital Tuebingen is conducting a clinical trial (NCT02011919) to evaluate the efficacy and tolerability of US-guided HIFU treatment of FA. Here, we report upon our preliminary experiences with the new method. So far all of the women treated with HIFU have reported high satisfaction and would undergo the procedure again. US-guided HIFU treatment is able to significantly reduce FA volume and to ease symptoms such as pain and discomfort. Our previous results demonstrate that HIFU is a promising new treatment option for breast FA and could become a routine treatment for selected FA in the near future.

Find the article online (German version)

https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-0042-102731

Ultrasound-guided high intensity focused ultrasound treatment of breast fibroadenoma a multicenter experience

R. Kovatcheva, JN. Guglielmina, M. Abehsera, L. Boulanger, N. Laurent, E. Poncelet

Journal of Therapeutic Ultrasound (2015) 3:1

Background

The aim of our multicenter study was to assess the clinical outcome and safety of ultrasound (US)-guided high-intensity focused ultrasound (HIFU) in patients with breast fibroadenoma (FA).

Methods

From May 2011 to February 2013, 42 women with 51 FA in one or both breasts were selected for treatment with US-guided HIFU. Eight of 51 FA were treated twice. Patients' age ranged from 16 to 52 years (mean 32 years). All patients with FA underwent core needle biopsy with histological confirmation. HIFU treatment was performed as an outpatient procedure under conscious sedation. Exclusion criteria were pregnant or lactating women, microcalcifications within the lesion at mammogram, history of breast cancer, previous laser or radiation therapy, and breast implant in the same breast. All patients signed written informed consent. After the treatment, follow-up US with volume evaluation was performed at 2, 6, and 12 months.

Results

The FA mean baseline volume was 3.89 ml (0.34–19.66 ml). At 2-month follow-up, the mean volume reduction was 33.2% ± 19.1% and achieved significance at 6-month (59.2% ± 18.2%, $p < 0.001$) and 12-month (72.5% ± 16.7%, $p < 0.001$) follow-up. Related side effects as superficial skin burn with blister-like aspect in three patients and hyperpigmentation over the treated area in one patient were transient and resolved spontaneously. In one patient, asymptomatic subcutaneous induration persisted at the end of the study.

Conclusions

US-guided HIFU treatment is an effective noninvasive method for the treatment of breast FA and well tolerated by the patients. Preliminary results are encouraging and show that HIFU could be an alternative to surgery for breast FA.

Find the article online:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4310188/

High-intensity focused ultrasound in breast pathology: non-invasive treatment of benign and malignant lesions

B. Cavallo Marincola, F. Pediconi, M. Anzidei, E. Miglio, L. Di Mare, M. Telesca, M. Mancini, G. D'Amati, M. Monti, C. Catalano, A. Napoli

Expert Rev. Med. Devices Early online, 1–9, 2014

Breast neoplasms are one of the leading causes of morbidity and mortality in women. Even if surgery is the treatment of choice, other forms of less invasive radical treatment are desirable. High-intensity focused ultrasound is already established as a valid non-invasive technique that ensures tumor ablation in various organs. The use of ultrasound or magnetic resonance guidance allows having some advantages such as the capability to treat tumors in moving organs or the possibility to have a real-time monitoring of the temperature increase. The aim of this paper is to report the use of high-intensity focused ultrasound technique with ultrasound and magnetic resonance guidance for the ablation of breast tumors, including both benign and malignant lesions.

Find the article online:

http://informahealthcare.com/doi/abs/10.1586/17434440.2015.986096?journalCode=erd

Abstracts of oral communications – 2016 ABDA

Treatment of breast fibroadenoma with high intensity focused ultrasound

Brenin D., Rochman C.

Background

Fibroadenomas are common, benign lesions of the breast. Current management of patients with fibroadenomas includes observation or surgical excision. The objectives of this study are to evaluate the safety and feasibility of Ultrasound guided High Intensity Focused Ultrasound (USgHIFU) delivered by the Echopulse device (Theraclion, Paris) for treatment of breast fibroadenomas. General patient safety, cosmetic outcome, tumor response, and patient experience are being assessed.

Materials and methods

Twenty female patients diagnosed with palpable breast fibroadenomas 1cm or larger are being enrolled in a single arm study and are undergoing treatment of their tumor utilizing the Echopulse device. Optimal energy per sonication is established for each patient by determining the minimal setting found to produce bubbles within the lesion as observed on real-time B-mode ultrasound. Patients will have tumors meeting the following criteria: Distance from the skin of ≤ 23 mm to the posterior border of the fibroadenoma, ≥ 5 mm from the anterior border of the fibroadenoma, and ≥ 11mm from the focal point of the HIFU treatment. The chest wall must be more than 1cm from the posterior margin of the tumor, and tumor volume must be between 0.3cc and 10cc. Subjects are evaluated immediately after treatment and at 3, 6, and 12 months.

Results

The study remains open to accrual. Enrolment at the time of the writing of this abstract is 16 patients. Six patients remain in follow-up. To date, there have been no grade 3 adverse events, nor skin burns, persistent changes in skin appearance, nor other significant toxicities/morbidities observed. The most common toxicity observed was pain (reported by 9 of 16 patients). Mean patient rated pain score during treatment on a scale from 0 to 100 was 17.8. Preliminary patient satisfaction was 4.65 on a scale of 1-5 (5 = most satisfied), 10 of 11 reported they would undergo the procedure again, and 11/11 reported they would recommend the procedure to a friend or family member. Reduction in the size of the palpable mass was reported by both the patient and evaluating physician in almost all cases. Similar findings were found on ultrasound in the majority of cases. Cosmesis was excellent, and unchanged from baseline in all cases.

Conclusions

To date, in study IDE #G130252, USgHIFU for treatment of fibroadenoma has been effective, well tolerated, and resulted in minimal toxicity.

Abstracts of oral communications – 2016 FUS Symposium

Treatment of breast fibroadenoma with high intensity focused ultrasound. Update of feasibility study IDE #G130252

Brenin D., Rochman C.

Background

Fibroadenomas are common, benign lesions of the breast. A minority of fibroadenomas will disappear without treatment, but most increase in size or remain unchanged. Current management of patients with fibroadenomas in the United States includes observation or surgical excision. Many patients find their fibroadenoma bothersome, and thus opt for surgical excision.

The objectives of this study are to evaluate the safety and feasibility of Ultrasound guided High Intensity Focused Ultrasound (USgHIFU) delivered by the Echopulse device (Theraclion, Paris) for treatment of breast fibroadenomas. General patient safety, cosmetic outcome, tumor response, patient experience, physician/operator experience, and device performance are being assessed.

Materials and Methods

Twenty female patients diagnosed with palpable breast fibroadenomas 1cm or larger are being enrolled in a single arm study and will undergo treatment of their tumor utilizing a computer-driven, continuously cooled, extra-corporal HIFU probe mounted on an arm moved by motors, and guided in real-time with an integrated ultrasound imaging scanner. The integrated probe is positioned by the operator and the lesion is imaged. Treatment planning is automated and presented for review and approval on an integrated computer screen. Optimal energy per sonication is established for each patient by determining the minimal setting found to produce bubbles within the lesion as observed on real-time B-mode ultrasound. Patients will have tumors meeting the following criteria: Distance from the skin of ≤ 23 mm to the posterior border of the fibroadenoma, ≥ 5 mm from the anterior border of the fibroadenoma, and ≥ 11mm from the focal point of the HIFU treatment. The chest wall must be more than 1cm from the posterior margin of the tumor, and tumor volume must be between 0.3cc and 10cc.

Subjects are assessed immediately after treatment and at 3, 6, and 12 months.

Results

The study remains open to accrual, the following are PRELIMINARY RESULTS, thus the denominators vary by data point: Enrolment at the time of the writing of the abstract is16 patients. Six patients remain in follow-up. To date, there have been no grade 3 adverse events, nor any skin burns, persistent changes in skin appearance, nor other significant toxicities/morbidities observed in the patients treated. Mean patient-rated pain score during treatment on a scale from 0 to 100 was 17.8. One patient has reported persistent mild pain at 6 months follow-up (2 on a scale from 0 to 100). The most common toxicity observed was pain (reported by 9 of 16 patients). Preliminary patient satisfaction was 4.65 on a scale of 1-5 (5 = most satisfied),10 of 11 patients reported they would undergo the procedure again, and 11/11 reported they would recommend the procedure to a friend

or family member. Reduction in the size of the palpable mass was reported by both the patient and evaluating physician in almost all cases. Similar findings were found on ultrasound in the majority of cases. Cosmesis can be excellent, and unchanged from baseline in all cases to date.

Conclusions

To-date, USgHIFU, delivered by the Echopulse device for treatment of breast fibroadenomas in the IDE G130252 study has been well tolerated by patients, resulted in minimal toxicity, and appears to have been effective.

Find the abstract online:

https://www.xcdsystem.com/fus2016/program/ - Breast Tumors

Long-term efficacy and tolerability of one or two US-guided HIFU treatment of breast fibroadenoma

Kovatcheva R., Vlahov J., Zaletel K., Stoinov J.

Background/Introduction

Breast fibroadenoma (FA) is the most prevalent benign tumour, accounting for up to 70% of benign breast lesions (1, 2). They affect females in the reproductive period with two peaks of incidence in the third and in the fifth decade of life. During the follow-up, a minority of FA decrease in size or disappear, more than half of them remain unchanged, and some of them significantly increase (3).

Ultrasound (US)-guided high-intensity focused ultrasound (HIFU) is the only non-surgical and non-invasive procedure, where thermal destruction is achieved by precisely delivered energy to the target, without interrupting skin integrity. Recently, a multicentre study established that US-guided HIFU treatment of 51 FA resulted in 72.5% volume reduction at 1 year (4).

The purpose of our study was to compare the long-term efficacy and tolerability of one or two HIFU treatments in patients with breast FA.

Methods

Twenty patients with 26 FA were selected for US-guided HIFU. The therapy was performed with the system EchoPulse (Theraclion, France) on an outpatient basis, in one or two sessions, under conscious sedation. FA volume was assessed before and followed up to 24 months after the last HIFU treatment. After each procedure, adverse events were evaluated. Written informed consent was acquired from all patients.

Results and Conclusions

In 19/26 FA (73.1 %) one HIFU was performed (group 1), whereas 7/26 FA (26.9 %) received second HIFU (group 2) 6-9 months (median, 7 months) after the first session. In group 1 and 2, FA volume decreased significantly at 1-month ($p<0.001$) and 3-month follow-up ($p=0.005$), respectively, and continued to reduce until 24-month follow-up ($p<0.001$ and $p=0.003$, respectively). At 24 months, mean volume reduction was 77.32 % in group 1 and 90.47 % in group 2 ($p=0.025$). Mild subcutaneous oedema was observed in 4 patients and skin irritation in 3 patients.

US-guided HIFU represents a promising non-invasive method with sustainable FA volume reduction and patient's tolerability. Although one treatment is highly efficient, the volume reduction can be increased with second treatment.

High intensity focused ultrasound in the treatment of breast fibroadenomata: Results of the HIFU-F trial

Peek M., Ahmed M., Scudder J., Baker R., Pinder S., Douek M.

Background

Breast fibroadenomata (FAD) are the most common breast lumps in women and are treated conservatively unless they are symptomatic in which case surgical excision is usually recommended. High intensity focused ultrasound (HIFU) is a non-invasive ablative technique that can be used to treat FAD but is associated with prolonged treatment times. In the HIFU-F trial, we evaluated the change in volume over time with circumferential HIFU treatment of FAD and compared this to no treatment (control).

Materials and Methods

Patients aged 18 years or older, diagnosed with symptomatic, palpable FAD visible on ultrasound (US) were recruited. Patients were treated using the US-guided Echopulse device (Theraclion, Malakoff, France) under local anaesthesia. Primary outcome measures included: reduction in symptoms, reduction in treatment time compared to whole lesion ablation; feasibility to achieve a 50% reduction in volume after six months and decrease in volume compared to an observation only group (control). This study received ethical approval (REC 13/LO/1221).

Results

HIFU treatment was performed on 20 patients (mean age 30.3 years, SD 7.5 years). Six out of eight patients who experienced pre-treatment pain had complete resolution of their symptoms six months post-treatment. All short-term complications (e.g. ecchymosis and erythema) completely resolved within the first month post-treatment without the need for intervention. Hyper-pigmentation was found at three months in six patients and persisted at six months in four patients although it was asymptomatic. Circumferential ablation significantly reduced the mean treatment time by 37.5% (SD 20.1) compared to whole lesion ablation. US demonstrated a significant mean reduction in FAD volume of 43.5% (SD 38.8%) (P = 0.016) in the HIFU group and this was also significantly greater than the 4.6% (SD 46.0%) reduction in volume observed in the control group at six months (P = 0.002).

Conclusions

Circumferential HIFU ablation of FAD is feasible, with a significant reduction in volume compared to control patients. It provides a simple, non-invasive, outpatient – based alternative management option for FAD.

Find the abstract online:

https://www.xcdsystem.com/fus2016/program/ - Breast Tumors

Treatment of thyroid nodules with echotherapy

THERACLION

Abstracts of relevant publications

Single-session High Intensity Focused Ultrasound (HIFU) Treatment in Large-sized Benign Thyroid Nodules

Brian Hung-Hin LANG; Yu-Cho WOO; Keith Wan-Hang CHIU
Thyroid; March 2017

Background

High intensity focused ultrasound (HIFU) is a new, promising thermal ablation technique in treating benign thyroid nodules but its effectiveness in larger-sized nodules has been less well-described. The present study aimed to evaluate the treatment efficacy (i.e. extent of shrinkage at 6-month) of large-sized benign thyroid nodules by ultrasound (USG)-guided HIFU ablation.

Materials and methods

After ethics approval, all consecutive patients who underwent HIFU ablation of a symptomatic benign thyroid nodule with ≥6 months follow-up were analyzed. Treated nodules were categorized according to their pre-ablation volume (<10 mL (group I), 10 – 30 mL (group II) and >30 mL (group III)). All treatments were performed using a USG-guided HIFU device (EchoPulse; Theraclion, Paris, France). After treatment, the nodule volume was measured by USG at 1-week, 1-month, 3-month and 6-month. Total energy delivered to each nodule (in KJ) and the time taken (in minutes) for that delivery were automatically recorded. Primary outcome was change in nodule volume after 6 months. Percentage nodule volume change = [Baseline volume – volume at 6-month]/[Baseline volume] * 100. Ablation success was defined as >50% volume reduction.

Results

Seventy-three nodules were treated successfully and followed for ≥6 months. The overall median 6-month volume reduction was 68.3% (22.77 – 96.50) %. At 6-month, group III had a significantly less volume shrinkage than group I (48.1% vs. 77.6%, p<0.001) and group II (48.1% vs. 67.9%, p=0.002). Also, the proportion of ablation success at 6-month in group III was significantly less than the other two groups (p<0.001). Pre-ablation nodule volume >30 mL (OR=7.813, 95%CI=1.908 – 32.258, p=0.004) and lower total energy per nodule volume (OR=3.313, 95%CI=1.113 – 9.688, p=0.029) were significant factors for less ablation success.

Conclusions

Single-session HIFU ablation was highly effective in causing shrinkage of benign thyroid nodules at 6-month but the extent of shrinkage for larger-sized nodules (volume >30 mL) was noticeably less than that of smaller-sized nodules. Both pre-ablation nodule volume and total energy per nodule volume were significant determinants of ablation success. For larger-sized nodules, additional HIFU treatment 3-6 months after initial treatment might be preferred over sequential treatment within the same session.

High-intensity focused ultrasound for thyroid nodule ablation: the evidence to date

R. D. Kovatcheva, K. Zaletel

Reports in Medical Imaging, 2017

Abstract

Thyroid nodules are common in occurrence and most of them are benign in nature. Some of these nodules are to be treated as they continue to grow or cause undesirable symptoms. Recently, several minimally invasive thermal ablation techniques have been introduced to overcome the complications of traditional methods such as surgery. High-intensity focused ultrasound (HIFU) is the latest advance in treatment modalities, which is a noninvasive procedure that permits localized target destruction without affecting the surrounding tissues. HIFU is currently used in the treatment of various solid malignant and benign tumors. The purpose of this review is to provide an introduction to the literature, principles, and advances of HIFU therapy of benign thyroid nodules, as well as to provide a discussion on its efficacy, complications, and future.

Find the article online:

https://www.dovepress.com/high-intensity-focused-ultrasound-for-thyroid-nodule-ablation-the-evid-peer-reviewed-article-RMI

US-guided High-Intensity Focused Ultrasound Ablation of Benign Solid Thyroid Nodules: Initial Clinical Outcomes

R. D. Kovatcheva, J. D. Vlahov, J. I. Stoinov, K. Zaletel

Radiology, 2015

Purpose

To assess the short-term efficacy and safety of ultrasound (US)-guided highintensity focused ultrasound (HIFU) ablation for treatment of benign solid thyroid nodules.

Materials and methods

This prospective study was approved by the institutional ethics committee; written informed consent was acquired. HIFU was performed in one session under US-guidance and conscious sedation in 20 euthyroid patients (mean age, 44.5 years) with benign solitary or dominant thyroid nodule. Thyroid nodule volume, US structure and Doppler pattern were assessed at baseline, 1 week, 1, 3 and 6 months after treatment. Adverse events associated with HIFU were evaluated. Statistical analysis was conducted by using repeated measures analysis of variance, Student's t-test, $\chi 2$ test and correlation analysis.

Results

Starting from 4.96 mL ± 2.79 (standard deviation), the mean nodule volume decreased to 3.05 mL ± 1.96 at 3-month follow-up (20 patients, $P < .001$) reaching 2.91 mL ± 2.43 by the 6th month (16 patients, $P < .001$). By then, the mean volume reduction was 48.7% ± 24.3 ($P < .001$). Isoechoic nodules showed greater reduction at 1 month as compared to the hypoechoic nodules (31.6 ± 18.1 vs 16.4 ± 8.6, $P = .053$). Nodules with markedly increased blood flow showed smaller volume reduction at 3 months if compared with less vascularized nodules (10.9% ± 14.5 vs 41.5% ± 20.3, $P = .054$). Minor transient complications (subcutaneous edema, mild skin redness) were observed in 2 patients.

Conclusion

Early data suggest that US-guided HIFU ablation is an effective and safe procedure for treatment of benign solid thyroid nodules. Initial US echogenicity and vascularization influence the ablation outcome.

Find the article online:

http://pubs.rsna.org/doi/10.1148/radiol.15141492

Localized thyroid tissue ablation by high intensity focused ultrasound: Volume reduction, effects on thyroid function and Immune response

H. Korkusuz, N. Fehre, M. Sennert, C. Happel, F. Grünwald

Röfo; 2015

Purpose:

The aim of this study was to assess the effectiveness of high intensity focused ultrasound (HIFU) in reducing thyroid nodule volume while preserving thyroid function as measured by immunological response.

Materials and methods:

12 patients (9 females) whose average age was 56.9 years (37 - 81) were treated with HIFU in an ambulatory setting. All patients had a single benign thyroid nodule treated in one HIFU session. The median nodular outline volume (NOV) was 3.4 ml (range 0.6 - 5.0 ml). The therapeutic ultrasound probe (Echopulse(®) THC900 888-H) used works with a frequency of 3 MHz, reaching temperatures of 80 - 90° C and a mean output between 87.6 and 192.8 W. To assess possible effects of HIFU on thyroid function, serum levels of triiodothyronine (T3), thyroxine (T4), thyrotropin (TSH), thyroglobulin (hTg) and antibodies against thyroglobulin (TAbs), thyrotropin receptors (TRAbs) and thyroid peroxidase (TPOAbs) were measured at enrollment, 24-hours post-HIFU treatment and at 3-month follow-up.Pre- post thyroglobulin reduction was measured to evaluate the success of ablation and the nodular outline volume (NOV) was evaluated at baseline and the 3-month follow-up to assess effectiveness.

Results:

All measured hormone levels were within normal ranges and remained stable ($p > 0.05$). No clinically meaningful immune reaction was induced ($p > 0.05$). Thyroglobulin serum levels increased significantly at 24 hours after ablation ($p < 0.05$) and decreased significantly at the 3-month follow-up ($p < 0.05$), returning to pre-ablative levels. The median reduction in nodular outline volume (NOV) was 55 % ($p < 0.05$).

Conclusion:

HIFU is a safe and effective alternative for treating benign thyroid nodules, while preserving thyroid function. Further investigations with multiple treatments should be conducted to evaluate whether additional treatments can achieve greater volume reduction.

Find the article online:

https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0035-1553348

Volume reduction of benign thyroid nodules three months after a single treatment with High-Intensity Focused Ultrasound (HIFU)

H. Korkusuz, N. Fehre, M. Sennert, C. Happel, F. Grünwald

Journal of Therapeutic Ultrasound, 2015; 3:4

Background

High Intensity Focused Ultrasound (HIFU) is a promising, non-invasive technique in treating benign thyroid nodules (TNs). The aim of this study was to evaluate the efficacy of HIFU to induce clinically meaningful shrinkage in benign, predominantly solid TNs and to identify variables that influence or predict the magnitude of TN volume reduction.

Methods

For each of 10 subjects, HIFU treatment was conducted on a single nodule. Nodular volume was measured sonographically at baseline and at three months post procedure. Nodular function and early treatment assessment was done scintigraphically.

Results

Median nodular volume reduction was 0.7 ml absolute and 48.8 % relative to pre interventional size ($p>0.05$). Absolute shrinkage was negatively correlated with the average treatment depth ($\tau= -0.61$, $p<0.05$). Absolute nodular volume was positively correlated with the scintigraphic nodular uptake reduction ($\tau= -0.66$, $p<0.05$).

Conclusions

HIFU treatment of benign predominantly solid TNs appears to be safe and effective for inducing nodular shrinkage. Despite potential for improvement, a single treatment session with HIFU is already a viable alternative to more standard methods. The feasibility of multiple HIFU treatments requires further investigation. Due to small sample size, the findings of this analysis need conformation by larger studies.

Find the abstract online:

http://www.jtultrasound.com/content/3/1/4/abstract

Early assessment of high-intensity focused ultrasound treatment of benign thyroid nodules by scintigraphic means

H. Korkusuz, N. Fehre, M. Sennert, C. Happel, F. Grünwald

Journal of Therapeutic Ultrasound 2014, 2:18, 2014

Background

High-intensity focused ultrasound (HIFU) allows to inflict intracorporal thermal lesions without penetrating the skin or damaging the surrounding tissue. This analysis intends to assess the magnitude of HIFU-induced ablations within benign thyroid nodules using scintigraphic imaging with 99mTc.

Methods

Ten cold, hot, or indifferent nodules were treated using multiple pulses of HIFU to induce temperatures of around 85°C within the ablation zone. Pre- and posttreatment, uptake values of 99mTc-pertechnetate or 99mTc-MIBI were recorded. The pre-post reduction of nodular uptake was evaluated to assess ablation magnitude.

Results

Relative nodular uptake in relation to total thyroidal uptake decreased after one session of HIFU in all cases. Median 99mTc-MIBI uptake reduction was 35.5% (ranging from 11% to 57%; $p < 0.1$), while 99mTc-pertechnetate scintigraphy showed a median uptake reduction of 27% (range 10% to 44%; $p < 0.1$). No major complications were observed.

Conclusions

HIFU appears to be safe and is an easy to perform means of thermal ablation. This study shows that HIFU treatment in thyroidal nodules can be evaluated by scintigraphic means shortly after the intervention. Due to small sample size, the exact magnitude of HIFU ablation efficiency in thyroidal nodules remains a value to be assessed in a larger study.

Find the article online:

http://www.jtultrasound.com/content/2/1/18

Local thyroid tissue ablation by high-intensity focused ultrasound: Effects on thyroid function and first human feasibility study with hot and cold thyroid nodules

H. Korkusuz, M. Sennert, N. Fehre, C. Happel, F. Grünwald

International Journal of Hyperthermia, Early Online: 1–6, 2014

Objective

The aim of this study was to assess whether high-intensity focused ultrasound (HIFU), a new and promising method for the treatment of benign hot and cold thyroid nodules using thermal ablation, has an impact on thyroid function, and to evaluate its feasibility in outpatient settings. Additionally, a possible difference in the treatment of solid and complex thyroid nodules was evaluated.

Method

Ten patients with one thyroid nodule each (six cold and four hot nodules) underwent HIFU in January 2014. Four nodules were solid and six nodules were complex. Serum levels of triiodothyronine (T3), thyroxine (T4), thyrotropin (TSH), thyroglobulin (hTg) and additionally antibodies against hTg (TAK), TSH receptors (TRAK) and thyroid peroxidase (TPO) were measured at enrolment and 24 h after the HIFU treatment. The pre- and post-thyroglobulin reduction was measured to evaluate the scale of ablation. In addition, patients' pain was recorded on a numeric rating scale from 0 to 10.

Results

The HIFU treatment did not affect thyroid function, since hormone levels stayed stable ($p < 0.05$). No serious immune reaction was induced. Thyroglobulin serum levels increased significantly ($p < 0.05$) and were correlated to the total energy emitted by HIFU ($p < 0.1$). The results of complex thyroid nodules did not differ from solid thyroid nodules. Similarly, the results of hot thyroid nodules did not differ from cold thyroid nodules. All patients tolerated the whole treatment and no severe complications were observed.

Conclusion

HIFU is a safe and effective method to treat benign, solid, complex, hot and cold thyroid nodules preserving thyroid function. Further developments of the system are needed to gain suitability for daily use

Find the abstract online:

http://www.ncbi.nlm.nih.gov/pubmed/25313977

High-Intensity Focused Ultrasound Ablation of Thyroid Nodules: First Human Feasibility Study;

O. Esnault, B.Franc, F. Ménégaux, A. Rouxel, E. De Kerviler, P. Bourrier, F. Lacoste, J.Y. Chapelon, L. Leenhardt

Thyroid, Volume 21, Number 9, 2011

Background

Thyroid surgery is common, but complications may occur. High-intensity focused ultrasound (HIFU) is a minimally invasive alternative to surgery. We hypothesized that an optimized HIFU device could be safe and effective for ablating benign thyroid nodules without affecting neighboring structures.

Methods:

In this open, single-center feasibility study, 25 patients were treated with HIFU with real-time ultrasound imaging 2 weeks before a scheduled thyroidectomy for multinodular goiter. Thyroid ultrasonography imaging, thyroid function, were evaluated before and after treatment. Adverse events were carefully recorded. Each patient received HIFU for one thyroid nodule, solid or mixed, with mean diameter ≥8 mm, and no suspicion of malignancy. The HIFU device was progressively adjusted with stepwise testing. The energy level for ablation ranged from 35 to 94 J/pulse for different groups of patients. One pathologist examined all removed thyroids.

Results:

Three patients discontinued treatment due to pain or skin microblister. Among the remaining 22 patients, 16 showed significant changes by ultrasound. Macroscopic and histological examinations showed that all lesions were confined to the targeted nodule without affecting neighboring structures. At pathological analysis, the extent of nodule destruction ranged from 2% to 80%. Five out of 22 patients had over 20% pathological lesions unmistakably attributed to HIFU. Seventeen cases had putative lesions including nonspecific necrosis, hemorrhage, nodule detachment, cavitations, and cysts. Among these 17 cases, 12 had both ultrasound changes and cavitation at histology that may be expected for an HIFU effect. In the last three patients ablated at the highest energy level, significant ultrasound changes and complete coagulative necrosis were observed in 80%, 78%, and 58% of the targeted area, respectively. There were no major complications of ablation.

Conclusion:

This study showed the potential efficacy of HIFU for human thyroid nodule ablation. Lesions were clearly visible by histology and ultrasound after high energy treatments, and safety and tolerability were good. We identified a power threshold for optimal necrosis of the target thyroid tissue. Further studies are ongoing to assess nodule changes at longer follow-up times.

Find the abstract online:

http://www.ncbi.nlm.nih.gov/pubmed/21834683

Minimally Invasive Ablation of a Toxic Thyroid Nodule by High-Intensity Focused Ultrasound;

O. Esnault, A. Rouxel, E. Le Nestour, G. Gheron, L. Leenhardt

AJNR Am J Neuroradiol (2010)

HIFU is used in the treatment of cancer (prostate, breast) and uterine fibroma but not yet in TNs. This case report describes the first successful ablation of a toxic TN with HIFU. TSH and radioiodine scan normalization were achieved without complications and maintained for 18 months.

HIFU treatment is a minimally invasive technique that may be an effective safe alternative to radioiodine or surgery in patients with toxic TNs.

Article available in full PDF version:

http://www.ajnr.org/content/31/10/1967.full.pdf

Localized ablation of thyroid tissue by high-intensity focused ultrasound: improvement of noninvasive tissue necrosis methods.

O. Esnault, B. Franc, J.Y. Chapelon

Thyroid. 2009 Oct;19(10):1085-91.

Background

Although thyroid nodules are frequently detected in patients during routine examinations, such nodules are rarely malignant. Surgical treatment of nodules is controversial because of the possible complications associated with surgery, and there is an unmet need for a minimally invasive alternative. We previously reported on a high-intensity focused ultrasound (HIFU) device that induced necrosis in ewe thyroids. This complementary study on 27 ewes evaluated the use of the device to produce thyroid lesions, characterized the HIFU-induced lesions on the thyroid and surrounding structures, and evaluated the safety and reproducibility of the method.

Methods

A spherical 3-MHz transducer that was coupled to a 5-MHz linear array ultrasound imaging probe was used to generate powerful acoustic waves to destroy thyroid tissue. Three series of experiments were conducted: thyroid lesion experiments (10 ewes), safety experiments (4 ewes), and reproducibility experiments (13 ewes). After fixation of the ewe's neck, tissue lesions were examined both macroscopically and histologically.

Results

First, individual pulsed acoustical waves were used to induce lesions in 19 thyroid lobes. In most lesions, there was coagulative necrosis that was replaced later by fibrosis. Macroscopic examination of adjacent organs revealed skin lesions and muscle injuries. A second series of experiments evaluated the consequences of HIFU pulsed waves on structures surrounding the thyroid to better characterize possible side effects of HIFU. Firings at the periphery of eight lobes revealed macroscopic lesions in the trachea of one ewe and superficial esophagus lesions in three ewes. The recurrent nerves were damaged bilaterally in one ewe that died from dysphagia 3 days after HIFU. Four ewes were found to have muscle injuries, but no skin lesions were observed. A third series of experiments evaluated the reproducibility of a HIFU prototype designed specifically for human use. Thyroid lesions were obtained in 25 of the 26 treated lobes. No damage to the nerves, trachea, esophagus, or muscles was observed. About 3 of the 13 ewes had superficial skin burns.

Conclusion

The results obtained in the ewe model show that thyroid lesions with a defined volume can be induced safely and suggest that the HIFU device is now ready for evaluation in humans.

High-Intensity Focused Ultrasound (Hifu) Treatment For Thyroid Nodules: Experimental And First Clinical Studies

O. Esnault, B. Franc, L. Leenhardt, A. Rouxel, F. Ménégaux, F. Lacoste
Proceedings ISTU 2006

Objective

Thyroid nodules are common and can only be removed by surgery. High-intensity focused ultrasound (HIFU) could be a possible minimally invasive alternative treatment. The aim of this study was to assess the feasibility of using HIFU to precisely ablate thyroid nodules without affecting neighbouring structures.

Methods

HIFU was generated by a 3-MHz spherical piezocomposite transducer moved across the target in a stepwise fashion. In a first clinical study 25 patients had their nodules treated with HIFU 2 weeks prior to plan thyroidectomy, using increasing energy. The last patients received a local anesthesia. The lesions were assessed by the pathologist.

Results

The histological lesions were clearly visible in most of the fully treated patients, particularly those who received higher energy. Superficial and reversible skin blisters were observed in 7 patients. The design of the treatment head was subsequently modified to eliminate such risk.

Conclusion

The patient trials confirmed the precision of the targeting and set the energy levels for safe thyroid nodule ablation with HIFU. Further study is needed to assess nodule's changes at longer follow-up.

Localized Ablation of Thyroid Tissue by High-Intensity Focused Ultrasound: an Alternative to Surgery?

O. Esnault, B. Franc, JY Chapelon, F. Lacoste

Proceedings ISTU 2005

Purpose

The aim of this study was to evaluate the feasibility of using a High-intensity focused ultrasound (HIFU) device to obtain a localized destruction of the thyroid with no damage to adjacent tissues.

Materials and methods

The ewe model was used because its thyroid gland is easily accessible with ultrasound. The animals were anaesthetized with 10 mg / kg IV injection of Penthothal. The HIFU pulses were generated by a 3-MHz spherical transducer under ultrasound guidance. Macroscopic and microscopic tissue lesions were identified after formalin fixation of the anterior part of the ewe's neck.

Results

After determining the optimal instrument settings to obtain localized thyroid ablation, the repeatability of the method was evaluated using a HIFU prototype designed specifically for human use: in 13 ewes (26 treated lobes), an average of 20 (range: 14–27) ultrasound pulses (pulse duration: 3 s) per lobe covering a mean volume of 0.5 cm3 (range: 0.3–0.7 cm3) were delivered. The ewes were sacrificed 2–5 weeks after treatment delivery. No damage to the nerves, trachea, esophagus or muscle was observed. Only 3 ewes suffered superficial skin burns. The desired thyroid lesions were obtained in 25/26 treated lobes, as demonstrated by fibrotic tissues, which replaced necrotic areas.

Conclusion: These results obtained in the ewe model show that thyroid lesions of defined volume can be induced safely and suggest that the HIFU device is now ready for human trials.

Abstracts of poster presentation – ETA 2016

Functional and serum thyroglobulin changes after US-guided HIFU ablation of benign solid thyroid nodules in euthyroid patients.

Kovatcheva R., Vlahov J., Zaletel K., Shinkov A., Stoinov J., Ivanova R.S., Kirilov G.

Objectives

High-intensity focused ultrasound (HIFU) ablation induces coagulative necrosis inside the treated target. Our purpose was to assess the changes in thyroid function and serum thyroglobulin (Tg) immediately and 3 months after HIFU treatment of benign thyroid nodules.

Material and methods

Fifteen euthyroid patients, mean age 45.6 years, with solitary or dominant benign solid nodule, were treated once with US-guided moving-beam HIFU (EchoPulse BEAMOTION, Theraclion), under conscious sedation. Serum TSH, FT4, FT3, and Tg were assessed before and 1 day, 1 week and 3 months after HIFU. Thyroid ultrasound was performed at baseline and at 3-month follow-up. Written informed consent was acquired from all patients.

Results

The mean basal volume was 2.98±1.59 ml, the total applied energy was 5.05±2.38 kJ with mean procedure duration of 23.11±13.41 minutes. One day and 1 week after ablation, the mean serum Tg increased significantly (19.2 ng/ml [range, 0.9-183 ng/ml] vs 383 ng/ml [range, 34-500 ng/ml] and 38.4 ng/ml [range, 5.9-500 ng/ml], respectively, p=0.0007) and returned to baseline at 3-month follow-up. Mean TSH decreased significantly 1 day after HIFU (p=0.004), but no significant differences were found at 1-week and 1-month follow-up, as well as for FT4 and FT3. The mean nodule volume decreased significantly at 3 months (2.03±0.93, p=0.005), with mean volume reduction of 27.7±17.3%. We found significant positive correlation between the total applied energy and FT4 (r=0.618, p=0.014), FT3 (r=0.580, p=0.023) and Tg (r=0.750, p=0.001) at 1 week, as well as between the volume reduction and FT4 (r=0.707, p=0.003) and FT3 (r=0.573, p=0.025) at 1 week. There was also a significant negative correlation between the Tg and the volume reduction at 3 months (r=-0.530, p=0.042).

Conclusions

US-guided beam-motion HIFU ablation reduces effectively thyroid nodule volume and has only transient influence on thyroid function and Tg. The dynamic of hormonal and Tg changes could serve as an effect-predictor of HIFU treatment.

Abstracts of oral communications – 2016 FUS Symposium

A prospective study on the efficacy of single high intensity focused ultrasound treatment of patients with benign symptomatic thyroid nodule

Lang B., Wong C., Lam H.

Background

Benign thyroid nodules are prevalent among the general population and some nodules may exhibit growth over time leading to compression symptoms or cosmetic concerns. Although surgery remains the treatment of choice for symptomatic thyroid nodule, it is associated with a 2%–10% risk of complications and requires a general anesthesia. The aims of the present study were to assess the efficacy of a single treatment of high intensity focused ultrasound (HIFU) in reducing benign thyroid nodule volume and to evaluate the changes in health-related quality of life (HRQL) following a single HIFU treatment.

Materials and Methods

After obtaining IRB approval, consecutive patients with symptomatic thyroid nodule were assessed for eligibility. Inclusions were nodule(s) (1) without signs of malignancy (i.e. no suspicious clinical and ultrasonic features and benign cytology on fine needle aspiration), (2) measuring ≥10 mm on ultrasound (USG) in three orthogonal dimensions, (3) amenable to HIFU. Exclusions were nodule(s) (1) measuring < 4 0mm (by largest dimension), (2) located < 2 mm from trachea, esophagus or recurrent laryngeal nerve (where ablation might pose thermal injury). Eligible patients were offered a choice of HIFU treatment, active observation or surgical resection. HIFU treatment was conducted with the USG-guided Echopulse (Theraclion SA, France). Primary outcome was a change in index thyroid nodule volume 6 months after HIFU. To have 80% power and 95% confidence interval (two-sided) to detect minimal important difference of 20%, 20 patients were needed. Assuming a 10% incomplete and withdrawal rate, 22 patients were required. Thyroid volume (mL) was assessed at baseline (i.e. before ablation) (Figure 1), 1-week, 3-month and 6-month (Figure 2) while HRQL was assessed by the Chinese version of the SF-12v2 at baseline and 6-month. The HRQL measured by eight domain scores and two summary scores (physical and mental component summary) was then compared between those who received HIFU and those who chose active observation (controls) at 6-month.

Results

Over this period, 22 (52.4%) chose to receive a single course of HIFU (HIFU group) while the other 20 patients chose to have active observation (controls). Among the HIFU group, the majority were females (90.9%) and the majority (77.3%) had their index nodule as the dominant nodule in a multinodular goiter. The mean base index nodule volume was 6.48 ± 4.34mL (range: 0.92 - 16.76mL). At 6-month following HIFU, the treated nodule volume decreased to 1.38 ± 1.31 mL (n=22, p < 0 .001). The average extent of nodule reduction was 71.58 ± 11.81% (range: 54.45 – 90.09%). However, there was no significant correlation between extent of 6-month volume reduction and basal volume (r=0.096, p=0.806), total treatment time (r=0.503, p = 0.168), total energy delivered (r=0.122, p = 0755) or mean delivered energy per treated volume tissue (r=0.150, p = 0.700).

Compared with controls, the HIFU group achieved a significantly greater improvement in four quality-of-life domains (17.57 ± 6.46, p = 0.009 for role physical; 18.01 ± 6.78, p = 0.011 for bodily pain; 24.77 ± 8.15, p = 0.004 for general health; 32.61 ± 8.93 for social functioning), and physical component summary of the SF-12v2 ((7.89 ± 2.83, p = 0.001).

Conclusions

USG-guided HIFU ablation is not only an effective and safe treatment option for patients with benign symptomatic thyroid nodules but has the potential of improving the HRQL of patients who do not wish to undergo surgical resection.

Find the abstract online:

https://www.xcdsystem.com/fus2016/program/ - Other Tumors

The effect of different treatment regimen with US-guided HIFU on thyroid nodule volume

Kovatcheva R., Vlahov J., Zaletel K., Stoinov J., Shinkov A.

Background/Introduction

Thyroid nodules can be detected by ultrasound (US) with a prevalence of 19-67%. Although 95% of them are benign, 1/3 show continuous growth and should be treated because of compression symptoms or cosmetic concerns (1). Surgery is still the main therapeutic strategy, in spite of the fact that it carries 2–10 % risk of complications (2).

US-guided high-intensity focused ultrasound (HIFU) is a non-invasive thermo-ablative method, developed to reduce thyroid nodule size (3, 4). The purpose of our work was to compare the long-term efficacy and safety of a single and repeated HIFU treatment of benign solid thyroid nodules.

Methods

Twenty euthyroid patients (mean age, 44.5 years) with benign solitary or dominant thyroid nodule were treated with US-guided HIFU system (EchoPulse, Theraclion, France) under conscious sedation. Twelve patients (group 1) received one treatment and 8 patients (group 2) repeated the treatment after 3 months of follow-up. US volume measurement was performed at baseline, 3 and 12 months after the final treatment. Adverse events were evaluated. Written informed consent was acquired from all patients.

Results and Conclusions

The baseline nodule volume and the energy applied per nodule volume did not differ significantly between group 1 and group 2 (5.04 ± 2.70 ml and 4.83 ± 2.74 ml, respectively; 3.5 ± 1.4 kJ/mL and 4.1 ± 1.6 kJ/mL, respectively). At 12-month follow-up the mean nodule volume decreased significantly in both groups (2.35 ± 2.44 ml, p=0.003, and 2.63 ± 1.85 ml, p=0.017, respectively) with a maximal volume reduction of 95.4% and 66%, respectively. The mean percent of volume reduction at M3 after the first HIFU and at M12 after the final HIFU differed significantly between group 1 and 2 (47.4%±20.8 vs 24.2%±15.8, p=0.02 at M3, and 55.5% ± 28.4 vs 46% ± 22, p=0.011 at M12). After the first treatment transient subcutaneous oedema and mild skin redness were observed in 2 patients and after the second treatment, one patient developed Horner syndrome , which resolved 6 months later.

In solid benign thyroid nodules, the effect of one and two consecutive HIFU treatments is comparable. Larger studies are needed to explain the different thyroid nodule susceptibility to HIFU ablation.