Endocrinology

Radiofrequency Ablation (RFA) for Benign Thyroid Nodules: Long-term Follow-up Results

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Although most thyroid nodules are benign, some nodules require treatment because of cosmetic reasons and subjective symptoms (1). Traditionally the treatment for benign thyroid nodules consists of surgery and levothyroxine medication, however both have many drawbacks. Radiofrequency ablation (RFA) is a method of thermal ablation to induce thyroid tissue necrosis and has been applied to various benign and malignant tumors with good results (2-6). In the thyroid gland, RFA has been applied to a recurrent thyroid cancer (7-8).

Recently several articles have been published for RFA of benign thyroid nodules and their initial results were promising (9-16). Jeong et al. (13) reported their initial experience with large series, 302 nodules in 236 euthyroid patients. The inclusion criteria of thyroid RFA were as follows: (1) the presence of subjective symptoms (foreign body sensation, neck discomfort or pain, compressive symptom) or cosmetic problems; (2) a poor surgical candidate or refusal to undergo surgery; (3) fine-needle aspiration cytology and US findings that were compatible with a benign nodule at least two separate times. The exclusion criteria were as follows: (1) follicular neoplasm or malignancy on fine needle aspiration (FNA); (2) a nodule with the US criteria for a malignancy (taller than wide, marked hypoechogenicity, macro and microcalcifications, spiculated margin) (17), although the result of FNA was a benign result; (3) previous radiation or operation history to the head and neck. Most nodules (n=212, 70.2%) were treated in a single session but 90 nodules (29.8%) required more than two sessions (two times, n=63; three times, n=20; four times, n=4; five times, n=2; six times, n=1). The mean volume reduction of treated nodules at 1, 3 and 6 months after RFA was 58.2%, 74.4% and 84.8%, respectively. A volume reduction greater than 50% was observed in 91.1% (n=275), and 84 (27.8%) index nodules had disappeared on the follow-up ultrasonography (US). On the follow-up US examination, well treated nodules showed marked decrease in size, the echogenicity of the nodule was lower than that observed before ablation, and the intra-nodular vascularity had disappeared.

Spiezia et al. (16) reported their 2-year follow-up experience with 94 elderly patients (66 nontoxic nodules and 28 toxic/pretoxic nodules). Sixty patients were treated in a single session and thirty-four patients required more than one session (two sessions in 25 patients, three sessions in 7 patients). The mean volume reduction of treated nodules at 1-month, 1-year and 2-year after RFA was 54%, 78.6% and 79.4%, respectively. Prior to RFA treatment 88 patients had pressure symptoms in the neck, 68 had difficulty in swallowing, and 75 patients had aesthetic complaints. The symptom score improved significantly from 3.4±0.2 at baseline to 0.3±0.08 at 12 months after RTA (p<0.001) and symptom control was well maintained during the second year in all patients. A complete disappearance of all symptoms was obtained in 83 of 94 patients. At the end of the follow-up period, thyroid function was completely normalized in the absence of methimazole therapy in 15 of patients with pretoxic nodules (100%) and 7 of 13 patients with toxic nodules.
Our thyroid team have been applied RFA to thyroid lesion from 2002 and we have suggested two important techniques (9-11,13,15,18). Those were “Trans-isthmic Approach Method” and “Moving Shot Technique”. Based on our previous experiences, we inserted an electrode under US guidance along the short axis of the nodule using the “Trans-isthmic Approach Method” and we treated the nodule using a “Moving Shot Technique”. An electrode approach is made from the medial to the lateral aspect of a targeted nodule through isthmus (Trans-isthmic Approach Method), the short axis of the nodule, and RFA is performed in a transverse ultrasound view. This method has several advantages over the long-axis approach (caudocranial or craniocaudal direction) and the vertical approach. The first advantage of the transisthmic approach is that the electrode passes through sufficient thyroid parenchyma to prevent a change in the position of the electrode tip during swallowing or talking and prevents leakage of hot fluid in cases of cystic nodules. Another advantage is clear visualization of the relations of the thyroid nodule, electrode tip, and recurrent laryngeal nerve to one another. Continuous ultrasound monitoring of this clear visualization of these relations minimizes the risk of injury to the recurrent laryngeal nerve.

Our thyroid team also proposed “Moving Shot Technique” for thyroid RFA (9-11,13,15). In the liver the RF electrode is fixed during the ablation. However thyroid gland is relatively small organ compared with liver therefore fixation of the electrode for a long time is dangerous. So we divided the thyroid nodule into multiple conceptual ablating units and ablation has been performed unit by unit. We made these conceptual units smaller on the periphery of the nodule as well as in the portion of the nodule adjacent to the critical structures of the neck. The units were much larger in the central safe portion of the nodule. Italian RFA group performed RFA using multitined expandable electrode and fixed electrode technique (12,16).

The complication rate was about 3% in our institution from 2002 to 2007 (voice change, hematoma, tumor rupture, first degree skin burn, transient thyrotoxicosis etc.). Most common complaint was pain. During the ablation, most of the patients complained of various degrees of pain at the ablated site, or pain radiating to the head, ear, shoulder, or teeth. The pain decreased when the generator output was reduced or turned-off during ablation and was easily controlled by oral analgesics during admission. All of the complications were recovered spontaneously. So there was no permanent complication case. Deandrea et al. (12) reported mild edema and cervical pain in several patients. Spiezia et al. (16) reported 13 of 83 patients complained of slight transient cervical pain that spontaneously disappeared; in 5 of 83 patients, fever up to 38°C was recorded that spontaneously regressed 24–36 hours after RTA.

In conclusion, thyroid RFA is effective and safe method for treating benign thyroid nodules.

Reference
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Diagnosis and Treatment for Thyroid Nodular Diseases

Opening Remark

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We have three main issues to discuss in this annual meeting
1. Thyroid ultrasound for benign and malignant thyroid diseases
2. Update information concerning radiofrequency ablation for thyroid nodular
3. Recommendation in fine needles aspiration cytology in thyroid nodules

Abstract:

During last year, we have more information about minimally invasive therapeutic procedures in medicine that have become very popular. The reasons included reducing risk compared to classic surgical treatment, easy recovery, less complications, and lower cost. One of these methods is ultrasonography-guided radiofrequency ablation (RFA). Low-level laser therapy was first reported in chronic autoimmune thyroiditis patients based on both ultrasound studies and evaluations of thyroid function and thyroid autoantibodies. The preliminary results reveal that low-level laser therapy promotes the improvement of thyroid function, as patients experienced a decreased need for LT4, a reduction in TPOAb levels, and an increase in parenchymal echogenicity.

Data concerning the accuracy of [(18)F]-fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography, ultrasonography, and enhanced computed tomography alone in the preoperative diagnosis of lymph node metastasis in patients with papillary thyroid carcinoma this year illustrated that ultrasonography of metastases in the central and lateral cervical lymph nodes might be the best methodology for determining the extent of surgical resection required to remove metastatic lymph nodes adequately in patients with papillary thyroid carcinoma. The power Doppler ultrasonography in depicting vascularity and to determine whether the combination of vascularity and suspicious gray-scale ultrasound features is more useful in predicting thyroid malignancy than are gray-scale features alone The results concluded that vascularity itself or a combination of vascularity and gray-scale ultrasound features was not as useful as the use of suspicious gray-scale ultrasound features alone for predicting thyroid malignancy. In contrast, systematic review was to obtain summary estimates of the diagnostic accuracy of color Doppler ultrasonography in predicting malignancy in thyroid follicular neoplasms suggested that absence of internal flow or predominantly peripheral flow indicates a low probability of thyroid malignancy in follicular neoplasm. There are 10 recommended references listed which were published during last year.

References:

The Application of Ultrasonography in Thyroid Benign/Malignant Disease

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Thyroid disorder is very common disease in Taiwan. We could look many big goiter due to iodine deficiency in 1950. By 1960, the symptom was relieved after adding iodine in salt. However, big goiter was replaced by occult nodular after iodine in salt. Patient could not find it by himself. Thyroid nodule is not easily find by general doctor except skilled &/or special training Dr. In general, thyroid cancer was low mortality. So it was not cause to take care it. Thyroid cancer has gradually increased in the world. The major pattern was still papillary thyroid cancer. Risk factors are still not unknown. Some reports have indicated that environmental radiation and pollution. However, some reports have found no obvious source. By palpation alone, the prevalence of thyroid nodules in the general population is 5%. The incidence of thyroid cancer increased from 3.6 per 100 000 in 1973 to 8.7 per 100 000 in 2002- a 2.4-fold increase (95% confidence interval [CI], 2.2-2.6; P<.001 for trend) in U.S. The possibility of cause factor of increasing thyroid cancer was directly association with diagnostic improvement.

Ultrasonography of thyroid is safety, noninvasiveness, nonradioactivity, effectiveness, and rapidness to detect thyroid disorder. However, to differentiate benign or malignant thyroid nodule is impossible before high-resolution & real-time ultrasonography development. For evaluation of thyroid nodule, we can collect information from clinical symptoms and signs to differentiate benign or malignant. The accurate diagnosis is still low. Fine-needle aspiration cytology can help to diagnosis. However, the sensitivity & specificity is still restricted by good experience of cytologist & skilled punctured Dr. For the science and technique, real-time & high-resolution ultrasonography can provide more accurate & more sensitivity to diagnosis benign or malignant thyroid disorder. The typical imaging of ultrasonography is need to analysis of hypoechogenicity, irregular margin, microcalcification, increased blood flow, taller than wide, and halo sign in nodule. If you can get assisted aspiration cytology, you can get more diagnosis. Ultrasonography is a good choice to primary evaluation of thyroid nodule.
Thyroid Doppler Ultrasonography in Taiwan

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The Doppler effect, discovered by physicist Christian Johann Doppler in 1842, is the basis for determining the velocity and direction of blood flow[1]. Color Doppler ultrasonography (CDU) is now widely available for clinical application. Hypervascularity is seen in thyroid parenchyma with autoimmune thyroid diseases (AITD)[2]. The appearance of “thyroid inferno” is described in thyrotoxic Graves’ disease[3].

The parameters of CDU included pulsatility index (PI), resistive index (RI), peak systolic velocity (PSV), and blood volume flow (VF)[4]. There were no significant differences between right and left thyroid arteries in RI, PSV and VF estimations[4,5,6]. Thyroid function has good correlation with PSV and parenchymal VF[7]. The cut off value PSV 25 cm/sec can be used to predictive hyperthyroidism vs. euthyroidism with sensitivity 0.8 and specificity 0.7[2].

Due to less noise interference, RI is a more reliable measurement than PI. The patients with RI values above 0.7 should undergo ablative therapy[8]. The blood flow of the superior thyroid artery is positively related to intra-thyroid microvessel density, glandular weight, and histopathologic microscopic pattern. Preoperative CDU may help to predict intra-operative blood loss during thyroidectomy in patients with Graves’ disease[9].

In 1974, Szilard developed first 3D image of fetus in uterus[10]. The parameters for thyroid size and vascular assessment included vascularization index (VI), flow index (FI), vascularization-flow index (VFI), were obtained using the virtual organ computer-aided analysis (VOCAL) program. 3D power Doppler ultrasonography with the VOCAL program is a reproducible tool for evaluating diffuse thyroid disorders due to an autoimmune process. The VI is the most reliable and less user-dependent parameter (intra-CC>0.8987 and inter-CC>0.8881) [11]. Right lobe of thyroid is larger in size and higher VI than left lobe in simple goiter but not AITD[12]. Mean thyroid size and 3 vascular indices of both lobes had good correlation with thyroid function. The cut off value VI=17.6% obtain good sensitivity(0.93) and specificity(0.91) for hyperthyroidism prediction (not published). The application of 3D ultrasonography in thyroid nodule will be in program.

Reference:
Debate of Thyroid Aspiration Cytology – Should All Nodular Goiters Receive FNAC

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Thyroid nodules are common clinical problems with high prevalence, approximately 5% in general population. Most of the thyroid nodules are benign; the malignancy rate is 7-15%. Fine needle aspiration cytology (FNAC) of suspicious nodule with or without ultrasound guidance is reliable to select patient requiring surgery. However, it is not cost-effective to perform FNAC on every thyroid nodule because of the high prevalence of thyroid nodules.

Many studies have been conducted to find out the sonographic features related to malignancy. These features include hypoechoegenicity, irregular margins, calcification, greater length than width, and solid echotexture. Thyroid pattern recognition to identify benign thyroid nodules was also developed recently. Four specific patterns: spongiform configuration, cyst with colloid clot, giraffe pattern, and diffuse hyperechogenicity, had 100% specificity for benignity. Familiar to the specific sonographic features and nodules pattern can help to reduce the unnecessary thyroid aspiration.

Ultrasonographic Differentiation between Kikuchi’s Disease and Lymphoma in Patients with Cervical Lymphadenopathy

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Background: Kikuchi’s disease, or histiocytic necrotizing lymphadenitis, is a self-limited necrotizing lymphadenitis. Clinically, it resembles lymphoma. We want to compare the sonographic features between Kikuchi’s disease and lymphoma in patients with cervical lymphadenopathy. Materials and methods: We collected 102 cervical lymphadenopathy samples (66 nodes from 11 Kikuchi’s disease patients and 36 nodes from 10 malignant lymphoma patients). The demographic and ultrasonographic characteristics of lymph nodes were retrospectively reviewed and analyzed. Results: The Kikuchi’s disease patients were younger than those with lymphoma. There was no difference in laterality of nodes. The ranges of Short-axis and Long-axis length were 7.1±2.8 mm (mean±SD) versus 13.2±4.6 mm and 13.3±5.7 mm versus 20.5±4.5 mm for Kikuchi’s disease versus lymphoma (p<0.01), respectively. The S/R ratio of Kikuchi’s disease nodes was 0.56±0.16 compared to 0.67±0.17 in lymphoma nodes (p<0.01). Thirty-six of sixty-six nodes (60%) of Kikuchi’s disease, and three of thirty-six nodes (8%) of malignant lymphoma had signs of cortical widening (p<0.0001). Twenty-seven nodes (41%) of Kikuchi’s disease and four nodes (11%) of malignant lymphoma were matted (p=0.001). Twelve of thirty-six nodes of lymphoma and five of sixty-six nodes of Kikuchi’s disease had features of micronodular reticular echotexture (p<0.01). All nodes exhibited hypoechoogenicity, and there was no difference in sharpness of border and presence of echogenic hilum between the two diseases (p>0.05). Conclusion: Analysis of basic ultrasonographic characteristics (size, shape, rims, matting and echotexture) help differentiate cervical lymph nodes in patients with Kikuchi’s disease and lymphoma. (Key words: Kikuchi’s disease, lymphoma, lymph nodes, neck, ultrasonography)
Real-time Fusion on Parathyroid Scintigraphy with Ultrasound: A Case Demonstration

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Background The two mostly widely used imaging techniques for pre-operative localization of parathyroid lesions are ultrasound and Tc-99m sestamibi scintigraphy. Ultrasound allows anatomical detection of an enlarged parathyroid gland; however, the presence of co-existing nodular thyroid disease reduces the sensitivity and specificity. Parathyroid scintigraphy with Tc-99m sestamibi, which was mainly taken up by mitochondria, has high sensitivity in detecting parathyroid adenoma, but relatively poor for multiglandular hyperplasia. Recent studies confirmed that the complimentary roles of ultrasound and scintigraphy and the highest sensitivity of combined tests. Here we report a case with secondary hyperparathyroidism referred for pre-operative localization of parathyroid lesions. Real-time fusion of scintigraphy with ultrasound was demonstrated. Materials and Methods 10 minutes and 2 hours after intravenous injection of 740 MBq of Tc-99m sestamibi, planar images of anterior, left anterior-oblique and right anterior-oblique views were obtained. SPECT/CT (Hawkeye4, GE healthcare, Israel) was also performed after the 2-hr scanning. The data of SPECT/CT was further processed by commercially available software (PMOD Ver. 3.11) to generate the positive sestamibi uptake on the co-registered CT images. The processed data were imported into the ultrasound scanner equipped with virtual navigation system (MylabTM70 XVG, Esaote, Italy). Results Two nodular lesions with positive uptake of Tc-99m sestamibi were noted within the bilateral thyroid beds on the SPECT/CT images. With the guidance of processed SPECT/CT images, the target lesions were rapidly localized on the sonography, showing as hypoechoic nodules, consistent with hyper-parathyroid lesions. Conclusion We firstly developed a method that successfully fused parathyroid scintigraphy in real-time with ultrasound and helped localize the parathyroid lesion more confidently. Further study should be warranted to confirm the clinical utility of parathyroid scintigraphy guided real-time virtual sonography in the diagnosis and management of hyperparathyroidism.
Preliminary Result on Real-time Fusion of Thyroid Scintitigraphy with Ultrasound

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Background Thyroid sonography provides high-resolution images for depicting the anatomy of thyroid gland. In contrast, thyroid scintigraphy provides unique functional information, which is proportional to the expression of sodium/iodine symporter (NIS) at the molecular level. Both imaging modalities are clinically used as the first-line diagnostic tests in the evaluating various kinds of benign or malignant thyroid diseases and provide complementary information. In this report, we first tried to import the thyroid scintigraphy into the real-time fusion ultrasound to integrate the information from both tests in a more detailed manner.

Materials and Methods
SPECT/CT was performed for the patient with a palpable nodule referred for thyroid scintigraphy using a hybrid gamma-camera/computed tomography system (Hawkeye4, GE healthcare, Israel). Because the currently available ultrasound scanner with fusing function can only accepted the data of CT or MRI, we generate fusion images of SPECT and CT using commercially available software (PMOD Ver. 3.11). Then the fusion images were captured slice by slice, converted to monochrome (gray scale) and saved as CT volume data. Finally, the data were imported into the ultrasound scanner equipped with virtual navigation system (MylabTM70 XVG, Esaote, Italy).

Results
The nodule was a hypofunctioning lesion (cold nodule) shown on the scintigraphy and the SPECT/CT images. The reformatted SPECT/CT volume data, combining the functional information of thyroid scintigraphy with anatomy information of CT, can be correctly displayed on the ultrasound scanner. The sternal notch was used as the reference point for registration. With the guidance of SPECT/CT images, the nodular lesion was rapidly localized on the sonography, showing as a hypoechogeneity mass, which fused with the SPECT/CT images perfectly.

Conclusion
Our method first successfully fused the thyroid scintigraphy with ultrasound. In addition to image fusion, needle aspiraton or even interventional therapy can also be further guided by thyroid scintigraphy using this method.