CHAPTER 1
History of Thyroid Ultrasound

Robert A. Levine

INTRODUCTION

The thyroid is well suited to ultrasound study because of its superficial location, vascularity, size, and echogenicity [1]. In addition, the thyroid has a very high incidence of nodular disease, the vast majority benign. Most structural abnormalities of the thyroid need evaluation and monitoring, but not intervention [2]. Thus, the thyroid was among the first organs to be well studied by ultrasound. The first reports of thyroid ultrasound appeared in the late 1960s. Between 1965 and 1970 there were seven articles published specific to thyroid ultrasound. In the last 5 years there have been over 2,200 articles published. Thyroid ultrasound has undergone a dramatic transformation from the cryptic deflections on an oscilloscope produced in A-mode scanning, to barely recognizable B-mode images, followed by initial low resolution gray scale, and now modern high resolution images. Recent advances in technology, including harmonic imaging, spatial compound imaging, contrast studies, and three-dimensional reconstruction, have furthered the field.

In 1880, Pierre and Jacques Curie discovered the piezoelectric effect, determining that an electric current applied across a crystal would result in a vibration that would generate sound waves, and that sound waves striking a crystal would, in turn, produce an electric voltage. Piezoelectric transducers were capable of producing sonic waves in the audible range and ultrasonic waves above the range of human hearing.

SONAR

The first operational sonar system was produced 2 years after the sinking of the Titanic in 1912. This system was capable of detecting an iceberg located 2 miles distant from a ship. A low-frequency

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audible pulse was generated, and a human operator listened for a change in the return echo. This system was able to detect, but not localize, objects within range of the sonar [3].

Over the next 30 years navigational sonar improved, and imaging progressed from passive sonar, with an operator listening for reflected sounds, to display of returned sounds as a one-dimensional oscilloscope pattern, to two-dimensional images capable of showing the shape of the object being detected.

EARLY MEDICAL APPLICATIONS

The first medical application of ultrasound occurred in the 1940s. Following the observation that very high intensity sound waves had the ability to damage tissues, lower intensities were tried for therapeutic uses. Focused sound waves were used to mildly heat tissue for therapy of rheumatoid arthritis, and early attempts were made to destroy the basal ganglia to treat Parkinson's disease [4].

The first diagnostic application of ultrasound occurred in 1942. In a paper entitled "Hyperphonagraphy of the Brain," Karl Theodore Dussic reported localization of the cerebral ventricles using ultrasound. Unlike the current reflective technique, his system relied on the transmission of sound waves, placing a sound source on one side of the head, with a receiver on the other side. A pulse was transmitted, with the detected signal purportedly able to show the location of midline structures. While the results of these studies were later discredited as predominantly artifact, this work played a significant role in stimulating research into the diagnostic capabilities of ultrasound [4].

Early in the 1950s the first imaging by pulse–echo reflection was tried. A-mode imaging showed deflections on an oscilloscope to indicate the distance to reflective surfaces. Providing information limited to a single dimension, A-mode scanning indicated only distance to reflective surfaces (see Fig. 2.7) [5]. A-mode ultrasonography was used for detection of brain tumors, shifts in the midline structures of the brain, localization of foreign bodies in the eye, and detection of detached retinas. In the first presage that ultrasound may assist in the detection of cancer, John Julian Wild reported the observation that gastric malignancies were more echogenic than normal gastric tissue. He later studied 117 breast nodules using a 15 MHz sound source, and reported that he was able to determine their size with an accuracy of 90%.

During the late 1950s the first two-dimensional B-mode scanners were developed. B-mode scanners display a compilation of sequential A-mode images to create a two-dimensional image (see Fig. 2.2). Douglass Howry developed an immersion tank

B-mode ultrasound system, and several models of immersion tank scanners followed. All utilized a mechanically driven transducer that would sweep through an arc, with an image reconstructed to demonstrate the full sweep. Later advances included a hand-held transducer that still required a mechanical connection to the unit to provide data regarding location, and water-bag coupling devices to eliminate the need for immersion [6].

THYROID ULTRASOUND

Application of ultrasound for thyroid imaging began in the late 1960s. In July 1967 Fujimoto et al. reported data on 184 patients studied with a B-mode ultrasound "tomogram" utilizing a water bath [7]. The authors reported that no internal echoes were generated by the thyroid in patients with no known thyroid dysfunction and nonpalpable thyroid glands. They described four basic patterns generated by palpably abnormal thyroid tissue. The type 1 pattern was called "cystic" due to the virtual absence of echoes within the structure, and negligible attenuation of the sound waves passing through the lesion. Type 2 was labeled "sparsely spotted," showing only a few small echoes without significant attenuation. The type 3 pattern was considered "malignant" and was described as generating strong internal echoes. The echoes were moderately bright and were accompanied by marked attenuation of the signal. Type 4 had a lack of internal echoes but strong attenuation. In the patients studied, 65% of the (predominantly follicular) carcinomas had a type 3 pattern. Unfortunately, 25% of benign adenomas were also type 3. Further, 25% of papillary carcinomas were found to have the type 2 pattern. While the first major publication of thyroid ultrasound attempted to establish the ability to determine malignant potential, the results were nonspecific in a large percentage of the cases.

In December 1971 Manfred Blum published a series of A-mode ultrasounds of thyroid nodules (Fig. 2.1) [5]. He demonstrated the ability of ultrasound to distinguish solid from cystic nodules, as well as accuracy in measurement of the dimensions of thyroid nodules. Additional publications in the early 1970s further confirmed the capacity for both A-mode and B-mode ultrasound to differentiate solid from cystic lesions, but consistently demonstrated that ultrasound was unable to distinguish malignant from benign solid lesions with acceptable accuracy [8].

The advent of gray scale display resulted in images that were far easier to view and interpret [9]. In 1974 Ernest Crocker published "The Gray Scale Echographic Appearance of Thyroid Malignancy" [10]. Using an 8 MHz transducer with a 0.5 mm resolution, he described "low amplitude, sparse and disordered echoes" characteristic of thyroid cancer when viewed with a gray scale display. The pattern felt to be characteristic of malignancy was what would now be considered "hypoechoic and heterogeneous." Forty of the eighty patients studied underwent surgery. All six of the thyroid malignancies diagnosed had the described (hypoechoic) pattern. The percentage of benign lesions showing this pattern was not reported in the publication.

With each advancement, in technology, interest was again rekindled in ultrasound's ability to distinguish a benign from a malignant lesion. Initial reports of ultrasonic features typically describe findings as being diagnostically specific. Later, reports follow showing overlap between various disease processes. For example, following an initial report that the "halo sign," a rim of hypoechoic signal surrounding a solid thyroid nodule, was seen only in benign lesions [11], Propper reported that two of ten patients with this finding had carcinoma [12]. As discussed in Chap. 6 the halo sign is still considered to be one of the numerous features that can be used in determining the likelihood of malignancy in a nodule.

In 1977 Wallfish recommended combining fine-needle aspiration biopsy with ultrasound in order to improve the accuracy of biopsy specimens [13]. Recent studies have continued to demonstrate that biopsy accuracy is greatly improved when ultrasound is used to guide placement of the biopsy needle. Most patients with prior "nondiagnostic" biopsies will have an adequate specimen when ultrasound-guided biopsy is performed [14]. Ultrasound-guided fine-needle aspiration results in improved sensitivity and specificity of biopsies as well as a greater than 50% reduction in nondiagnostic and false negative biopsies [15].

In the 1980s the utility of thyroid ultrasound became evident. Within 4 years after the Chernobyl nuclear accident, the incidence of papillary thyroid cancer increased 100-fold among young children in areas of high radiation exposure. Ultrasound screening of these children detected thousands of patients with early thyroid cancer and allowed surgical cure. Screening continues to be performed on this population, and the death rate from thyroid cancer among these individuals remains nil. Ultrasound screening has also been demonstrated to be of value in patients with relatives having familial papillary or medullary thyroid cancer.

Ultrasound also has a useful role in population screening for iodine deficiency. Ultrasound provides a simple and accurate way to measure thyroid gland volume. It has been shown that thyroid volume in children correlates well with both dietary iodine content and urinary iodine excretion. Thus ultrasound provides an efficient method of identifying iodine deficient areas of the world. Ultrasound screening has proven easier to accomplish and as accurate as 24 h urine collection, and has expedited the treatment of endemic goiter.

Current resolution allows demonstration of thyroid nodules smaller than 1 mm; thus ultrasound has clear advantages over palpation in detecting and characterizing thyroid nodular disease. Nearly 50% of patients found to have a solitary thyroid nodule by palpation will be shown to have additional nodules by ultrasound, and more than 25% of the additional nodules are larger than 1 cm [16]. With a prevalence estimated between 19 and 67%, the management of incidentally detected, nonpalpable thyroid nodules remains controversial [17]. Several guidelines have been developed to assist in deciding which nodules warrant biopsy and which may be monitored without tissue sampling. These guidelines are discussed in Chap. 7.

Over the past several years the value of ultrasound in screening for suspicious lymph nodes prior to surgery in patients with biopsy proven cancer has been established. Current guidelines for the management of thyroid cancer indicate a pivotal role for ultrasound in monitoring for loco-regional recurrence [17].

During the 1980s Doppler ultrasound was developed, allowing detection of flow in blood vessels. As discussed in Chap. 3 the Doppler pattern of blood flow within the thyroid nodules may play a role in assessing the likelihood of malignancy. Doppler imaging may also demonstrate the increased blood flow characteristic of Graves' disease [18], and may be useful in distinguishing between Graves' disease and thyroiditis, especially in pregnant patients or patients with amiodarone-induced hyperthyroidism [19].

Recent technological advancements include intravenous sonographic contrast agents, three-dimensional ultrasound imaging, and elastography. Intravenous sonographic contrast agents are available in Europe, but remain experimental in the United States. All ultrasound contrast agents consist of microspheres, which function both by reflecting ultrasonic waves and, at higher signal power, by reverberating and generating harmonics of the incident wave. Ultrasound contrast agents have been predominantly used to visualize large blood vessels, with less utility in enhancing parenchymal tissues. They have shown promise in imaging peripheral vasculature as well as liver tumors and metastases [20], but no studies have been published demonstrating an advantage of contrast agents in routine thyroid imaging. The use of contrast agents may be helpful in the early assessment of successful laser or radiofrequency ablation of thyroid nodules [21].

Three-dimensional display of reconstructed images has been available for CT scan and MRI for many years and has demonstrated practical application. While three-dimensional ultrasound has gained popularity for fetal imaging, its role in diagnostic ultrasound remains unclear. While obstetrical ultrasound has the great advantage of the target being surrounded by a natural fluid interface, greatly improving surface rendering, three-dimensional thyroid ultrasound is limited by the lack of a similar interface distinguishing the thyroid from adjacent neck tissues. It has been predicted that breast biopsies may eventually be guided in a more precise fashion by real time three-dimensional imaging [22], and it is possible that, in time, thyroid biopsy will similarly benefit. At the present time, however, three-dimensional ultrasound technology does not provide a demonstrable advantage in thyroid imaging.

Elastography is a promising technique in which the compressibility of a nodule is assessed by ultrasound while external pressure is applied. With studies showing a good predictive value for prediction of malignancy in breast nodules, recent investigations of its role in thyroid imaging have been promising. Additional prospective trials are ongoing to assess the role of elastography in predicting the likelihood of thyroid malignancy. The role of elastography in the selection of nodules for biopsy or surgery is discussed in Chap. 15.

With the growing recognition that real time ultrasound performed by an endocrinologist provides far more useful information than that obtained from a radiology report, office ultrasound by endocrinologists has gained acceptance. The first educational course specific to thyroid ultrasound was offered by the American Association of Clinical Endocrinologists (AACE) in 1998. Under the direction of Dr. H. Jack Baskin, 53 endocrinologists were taught to perform diagnostic ultrasound and ultrasound-guided fine-needle aspiration biopsy. By the turn of the century 300 endocrinologists had been trained. Endocrine University, established in 2002 by AACE, began providing instruction in thyroid ultrasound and biopsy to all graduating endocrine fellows. By the end of 2011 over 4,000 endocrinologists had completed an AACE ultrasound course. In 2007 a collaborative effort between the American Institute of Ultrasound in Medicine and the AACE established a certification program for endocrinologists trained in neck ultrasound. By the end of 2011 the ECNU (Endocrine Certification in Neck Ultrasound) program had certified over 200 endocrinologists as having the training, experience, and expertise needed to perform thyroid and parathyroid ultrasound and fine needle aspiration biopsy. In 2011 the American Institute of Ultrasound in

Medicine began accrediting qualified endocrine practices as centers of excellence in thyroid and parathyroid imaging.

In the 40 years since ultrasound was first used for thyroid imaging, there has been a profound improvement in the technology and quality of images. The transition from A-mode to B-mode to gray scale images was accompanied by dramatic improvements in clarity and interpretability of images. Current high resolution images are able to identify virtually all lesions of clinical significance. Ultrasound characteristics cannot predict benign lesions, but features including irregular margins, microcalcifications, and central vascularity may deem a nodule suspicious [3]. Ultrasound plays a clear fundamental role in thyroid nodule evaluation and the selection of which nodules should undergo biopsy. [17] Ultrasound has proven utility in the detection of recurrent thyroid cancer in patients with negative whole body iodine scan or undetectable thyroglobulin [17, 23]. Recent advances including the use of contrast agents, tissue harmonic imaging, elastography, and multiplanar reconstruction of images will likely further enhance the diagnostic value of ultrasound images. The use of Doppler flow analysis and elastography may improve the predictive value for determining the risk of malignancy, but no current ultrasound technique is capable of determining benignity with an acceptable degree of accuracy. Ultrasound guidance of fine-needle aspiration biopsy has been demonstrated to improve both diagnostic yield and accuracy, and is becoming the standard of care. Routine clinical use of ultrasound is often considered an extension of the physical examination by endocrinologists. High quality ultrasound systems are now available at prices that make this technology accessible to virtually all providers of endocrine care [3].

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