AN ILLUSTRATED NARRATIVE OF THE DISCOVERY OF ULTRASONIC SOFT-TISSUE ECHOING IN 1949 AND ITS SUBSEQUENT MEDICAL APPLICATIONS

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Several non-invasive, imaging techniques have been developed to aid the clinician in diagnosing disease: x-radiation, nuclear medicine, thermography, magnetic resonance and ultrasound. For tumor detection and diagnosis these techniques are highly dependent upon the adequacy and operation of particular machines, on visual responses of the human eye and on the clinician's skills for subjectively identifying an abnormality. Of the medical imaging techniques most frequently used, diagnostic ultrasound is safe with regard to causing physical and genetic effects. Furthermore, use of ultrasonic techniques offers the potential not only for rapid localization of tumors but also for exploiting its tissue characterization capabilities for detecting and diagnosing certain types of neoplasms quantitatively – that is, without the need for subjective evaluation by a trained clinician. This linkage of ultrasonic detection/diagnostic possibilities – safety plus quantitative objectivity – is my future hope for a new system of effective, safe, cost-effective per-case-found, mass-screening for breast and other short range cancer sites; an urgent need in our current health care delivery system. In this presentation an attempt will be made to describe empirical biological experiments leading ultimately to a means of mass population screening of the breast and gastro-intestinal tract.

A broad background education in natural sciences at Cambridge University and training in clinical medicine at University College Hospital in London, England, as part of Cambridge's medical degree program, provided the necessary qualifications for my undertaking medical investigations of acute human bowel crises while practicing surgery in London during the early 1940's. This background education and experience led to an offer, and acceptance by me in 1946, of a post-doctoral fellowship in the Department of Surgery, University of Minnesota, where in 1949 my continuing work on human bowel failure prompted inquiry into the feasibility of using pulse-echo ultrasound for measuring the thickness of bowel wall, in an effort to diagnose various types of bowel failure for determining preferred treatment and prognosis.

Early in 1949 consultation with a senior research staff member of Minneapolis Honeywell Regulator Company produced access to an operational 15 MHz naval flight trainer at a nearby navy airbase. The trainer was capable of both A-mode trace (time-amplitude) presentations and real-time, two-dimensional B-mode readout options, but only the A-mode function was readily available for my use. An experiment using dog bowel was designed to test whether the distance between inner and outer bowel wall could be resolved at 15 MHz using this existing equipment. Basic to further experimentation was construction of a small transducer chamber – not a difficult task, given my natural aptitude for mechanical engineering design and instrument fabrication. Success in these initial experiments, measuring soft tissues with pulse-echo ultrasound, led to the need for establishing a simple test procedure for use by the naval technician for adjusting the flight trainer from long to short-range A-mode operation for conducting future biological experiments. A naturally composite standard biological test specimen of 1mm of fresh beef muscle and 9mm of structural beef fat was arrived at by trial and error. A-mode examination of the test specimen proved echoing from gross anatomical boundaries and from within histological structure. By chance a surgical specimen of human stomach containing a cancerous ulcer became available. Significant echo changes were noted as the ultrasonic beam traversed areas nearing the tumor where cancerous invasion had been detected by palpation. Examination under a variety of positionings revealed differential sonic properties of carcinomatous tissue. These experiments proved scientifically that cancerous tissue reflected and attenuated ultrasound.

A paper reporting these experiments written in November 1949 was published in SURGERY in February 1950, the first in the scientific literature on soft tissue ultrasonic echo production. The discovery of differential acoustic properties of a cancerous stomach ulcer was a tremendous breakthrough in the dismal outlook for cancer in general at the time. I immediately saw the possibilities of harmless non-invasive examination of gross anatomical and histological structure in the living organism, both statically and kinetically. As a physician I chose to follow up the most urgent possibility of examining the breast and gastro-intestinal tract, since my acoustic equipment at high frequency was available in the form of 15 MHz quartz transducer capsules being supplied to the naval establishment. Experimentation continued at the naval base to confirm my primary tumor findings on malignant neurological tissue, checking for possible damage, and application clinically to two living, intact breast tumors in a clinical setting. The work up to this stage encouraged funding to enable construction in 1951 of a portable clinical pulse-echo ultrasonic instrument into which sector B-mode prototype capability was incorporated for producing images in real-time, a necessity for examining living patients under clinical conditions. A series of 20 breast lumps were examined using the biological technique of controlling for multiple variables comparing A-mode traces of breast lumps with those of normal breast tissue in a comparable position. Analysis of these traces revealed a numerical ratio of comparison between cases and the existence of a natural, quantitative sonic energy contrast between neoplastic growths and the normal surrounding tissue in the same individual. This finding was confirmed by the sector B-mode instrument both for living intact tumors and for gross normal anatomical structure. This work justified the construction of equipment for direct linear B-mode and other radar presentations to be tested at suitable accessible clinical sites such as the breast and lower gastro-intestinal tract using the available 15 MHz transducers. The scope of clinical application was, at this time, limited by fundamental frequency-range problems and the state of the art of piezo-electric materials.

In May 1953 the development of a self-contained, hand-held linear B-mode instrument made possible production of the *first real-time image* of a living, intact malignant tumor. This 7mm growth had been clinically diagnosed as "inflamed nipple". A similar image has yet to be produced with present-day equipment. Since 1953 it has been possible to detect neoplasms in the nipple-areola of the breast (25% of all breast malignancies) with this instantaneous, subjective visual readout system. A subsequent clinical series of 117 cases of breast lumps examined with a dedicated linear B-mode instrument produced a positive predictive index for malignancy in which predictive diagnosistic accuracy has yet to be matched by other workers. Small breast tumors of various types were all visualized answering the scientific question as to the possibility of use of the technique for detection. Tumors were imaged in both negative and positive contrast to the normal background tissue speckle. In both contrast types of malignant tumors, compression of tissue speckle in the area of the tumor image closest to the skin was observed. This observation was construed as detection of infiltration by cancer cells. Thus it was considered that detection and diagnosis of small glandular breast nodules would be highly probable with an objective system with electronic signal processing.

Such equipment was produced in December 1963 which could ultrasonically sweep the breast and compute sonic energy returns at a scanning speed of 1/2000 second. This system would enable rapid interrogation of normal and abnormal histological tissue to detect small volumes of ectopic tissue.

Pulse-echo ultrasound should be successful in objectively finding cancerous tumors, at least at common sites, on a screening basis. There remain many further applications of this safe form of radiation to be explored and developed for the benefit of mankind.