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THE TRANSFER OF TECHNOLOGY TO MEASURE SKIN BURN DEPTH IN HUMANS

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INTRODUCTION

This technology transfer has two origins. The idea of using ultrasound to measure burn wound depth came from foundational work performed by Dr. Cantrell and others (1, 2) at Oak Ridge National Laboratory. The ultrasonic instrumentation technology came from an area which was developed at NASA Langley Research Center for improved resolution of ultrasonic nondestructive evaluation equipment to locate cracks in metal structures. The combination of the work in both areas has led to the development of a device that can detect burn-wound depth in humans.

While details will vary among technology utilization projects, this project points to a model paradigm for the case where the technology transfer involves measurements with subtle and, initially, often hidden meanings and interpretations. It is absolutely essential to under stand the meaning of the measurements taken in the area of the transfer, and this must become a key ingredient in the transfer process.

We begin with a brief, somewhat simplified description of skin tissue. Skin tissue is the external covering of the body, whose functions include protection against injuries and parasitic invasion, and the regulation of body temperature. It is made up of essentially two layers. The outermost layer, the epidermis, consists mostly of layers of cells which are flattened toward the outside. The innermost layer, the dermis, contains a variety of structures, such as nerves, nerve endings, sweat glands, blood vessels, and hair follicles. Capillaries provide nourishment and essential fluids for the skin. An important structural component for skin is collagen, a very large protein molecule that in the normal state is coiled. We start with the fact that skin is a medium through which ultrasonic waves can pass.

THE FUNDAMENTAL STUDY

Central to any application of ultrasonic technology is a property of the medium or propagation called acoustic impedance. This is defined as the product of mass density and the sound velocity as shown in the equation,

$$Z = \rho v \qquad (1)$$

If the acoustic impedance remains constant along the propagation path of the ultrasonic wave, the wave will continue to propagate through the medium. If, however, the acoustic impedance changes abruptly or discontinuously, the situation shown in Figure 1 occurs.

An incident wave is considered one that propagates from left tot right in medium 1 and is characterized by a given constant value of the acoustic impedance. The wave propagates through medium 1 and a second medium 2 which is characterized by a different value of the acoustic impedance. The abrupt change is the acoustic impedance at the interface causes part of the incident wave to be reflected back through medium 1 toward the ultrasonic source. The remaining part of the wave is transmitted through the interface into medium 2. There is interest only in that part of the wave reflect back through medium 1 to the ultrasonic source since in the assessment of burn depth there is access only to one side of the skin tissue.

An experimental arrangement as this, whereby one sends out an ultrasonic pulse and "listens" for reflections or echo signals from interfaces is descriptively called the ultrasonic pulse-echo technique. The amount of the incident wave intensity reflected in the echo signal is directly proportional to the square of the difference in the acoustic impedances,

$$I_r = \left(\frac{Z_1 - Z_2}{Z_1 + Z_2}\right)^2 I \quad , \qquad (2)$$

Where I_r is the intensity of the reflected wave, and I is the intensity of the incident wave, and the subscripts designate the medium. For the case of burned tissue, medium 1 represents necrotic tissue and medium 2 the underlying viable tissue. If the differences in the acoustic impedances of the necrotic and viable tissues are sufficiently large to obtain a signal from the necrotic/viable tissue interface that is strong compared to background reflections then the technique would provide a potentially quantitative measure of burn depth.

Another acoustic property of a medium that can affect the intensity of a received ultrasonic signal is the attenuation of the medium. Attenuation causes a decrease in intensity as the ultrasound travels through the medium. It depends on various factors, including ultrasonic frequency. The effect can be written as

$$I = I_0 e^{-2\alpha x} \quad , \qquad (3)$$

where α is the attenuation coefficient, x is the thickness traversed, and I_0 is the intensity of ultrasound at $x = 0$.

The Initial Tests

An ultrasonic pulse-echo system of sufficient resolution was assembled to see if, indeed, it would be possible to use ultrasound to investigate burn wound depth. Figure 2 (right side) is an ultrasonic reflection from a burn wound site on a Yorkshire pig. A transducer, sitting atop a column of gel used as a medium to transmit the ultrasound between the transducer and the skin, is used to interrogate the burn site. As can be seen from the ultrasonic trace, a strong echo is received from the interface of the ultrasonic gel and skin surface. After a series of closely spaced reflections from the necrotic tissue, a reflection from the burn interface is observed, as are reflections from the dermis-fat interface and other interfaces within the skin. For comparison the ultrasonic echo is juxtaposed with the histological cross-section made from excised tissue from the same wound.

One can see the effects of both reflection and attenuation in the ultrasonic trace. The reflection from the gel-skin surface is the first reflection received and the largest. Other reflections or echoes received decrease in prominence partly because as they traverse greater distances in the skin, they become weaker.

An analysis of the data collected compared as shown in Figure 2 gave excellent agreement between burn depth measured by histologic cross-section and measurements of the ultrasonic reflection from the necrotic-viable tissue interface. The average deviation between the two sets of measurements is 2.2% with a maximum deviation of less than 5%. To within the uncertainties of the measurements, the ultrasonic technique can be used as reliably as histologic sectioning in the measurement of skin-burn depth in porcine skin, which physiologically similar to human skin.

The Theoretical Model

Other information about the nature of a burn wound was also obtained from constructing a theoretical model of the burn process (3). Separate heat conduction equations were written for the necrotic region and the viable region separated from the necrotic region by a plane. The skin surface was assumed to be held at 100° C, while the initial temperature of the skin was 35° C. When experimental data was substituted into the model, the temperature of the interface between the necrotic region and the viable region was calculated to be 65.3^0 C. This temperature is in agreement with the asymptotic temperature measured by Moritz and Henriques (4, 5) for the time-temperature relationship for thermal necrosis of porcine skin.

Also calculated from this model was the energy of transition of the collagen. A value of 11.7 cal/gm of collagen in skin tissue was obtained. The value of 11.7 cal/gm is consistent with other measurements of transition energies (enthalpy changes) of collagen from other sources (6-9). This is still another indication that the collagen phase transition plays a key role in burn necrosis.

Further studies in the role of collagen in burn injury were conducted by others. One of significant importance to our work was done by Bartos (10), who used an optical polarization technique to measure effects on the collagen in the burn wounds in Wistar rats to characterize thermal injury. From his studies he showed that at the collagen shrinkage temperature (63-66^0 C) collagen fibers lose their birefringence. He further notes that "collagen fibers destroyed by heat can no longer fulfill their physiological function; the corium becomes necrotized, and has to be removed and replaced by new connective tissue."

The role of collagen in skin necrosis is a primary one: As the skin necrotizes, the collagen undergoes a phase transition, or "melts," resulting in a difference in skin density between the viable state and the necrotic state. This gives rise to a difference in acoustic impedances between the two states. Examination of Equation 2 shows that an ultrasonic reflection occurs at this interface, which is the basis of the acoustic reflection shown and marked in Figure 1. According to Bartos this interface also divides the necrotic skin, which cannot support the process of healing, from the viable skin where healing processes can occur. This explains why the ultrasonic reflection from the necrotic-viable skin interface coincides with the histologic results.

The Role of Other Reflections

Other significant reflections from interfaces in skin are found. Reflections from the dermis-fat interface and the interface between the ultrasonic couplant (gel) and the from surface of the skin can be used in the process to correctly identify the reflection from the necrotic-viable skin interface. Using reference data for the acoustic impedance, we calculated the relative intensity of the reflections from each of the interfaces. Also of importance to the design was a knowledge of the range of attenuation in skin. According to Equation 3, the signals attenuate or decrease as they pass through the skin. The strength of the attenuation is expressed as α : the larger α , the greater the effect. A literature search was conducted to determine the attenuation of skin. Since attenuation varies with frequency, we also researched the attenuation's frequency dependence for skin.

The results of these investigations and calculations lead to the following prediction: if one applies a variable gain ultrasonic system in just the right amount to compensate for the attenuation of the ultrasonic signal as it passes though the skin, then the three major reflections (gel-skin surface interface, necrotic-viable skin interface, and the dermis-fat interface) will appear as reflections of nearly equal height (A specialized circuit to accomplish this is called a time-gain compensation circuit, or abbreviated TGC.). Consequently, by adjusting the parameters of the TGC one could bring the signal level of the reflections from the gel-skin surface and the dermis-fat interface to the same height. If set up in this way, the appearance of the echo from the necrotic-viable skin interface would always appear to be approximately the same height as the other two reflections despite the burn thickness. This is a very important point, since normally reflection intensities decrease the deeper into the skin that the necrotic-viable skin interface is located. Other reflections can consequently confuse the interpretation, unless an easily reproducible criterion is established. The success of making a clinically useful instrument hinged on this point. Without a means of clear and unequivocal interpretation, the instrument would be essentially useless in a clinical setting.

THE INSTRUMENTS REQUIREMENTS

Our first consideration was that the frequency would be high enough that the resolution would be better than 100 microns in skin tissue. This determined the minimum frequency response needed from the transducer. Once determined, the decision of the frequency characteristics of the system electronics could be made. The estimated range of attenuations found in the literature for measurements in skin helped to determine the overall gain requirements.

The first consideration was whether a commercial medical ultrasound machine existed with the requisite frequency response and TGC that could be used. All that we tested indicated that no commercial instrument on the market at the time could meet the requirements without substantial modification. We decided to examine the instrumentation available for use with nondestructive evaluation of material. We were able to purchase a basic pulse-receiver unit with a 60 MHz bandwidth, which we modified with a time-gain compensator of in-house design. The frequency response of the assembled unit was better than 50 MHz, with accurate and adjustable, truly exponential time-gain compensation throughout the frequency range.

The output from the modified pulser-receiver was connected to a storage oscilloscope to complete the A-scan ultrasonic system. The display on the oscilloscope face was an important consideration. We wanted the scan to cover a sufficient portion of the screen in order that measurement accuracy would not be adversely affected. We developed a circuit that triggered the oscilloscope upon receiving the reflection from the gel-skin interface. A delay line was added to the system in order that the beginning portion of the reflection from the gel-skin surface interface could be observed. Therefore, when the system was appropriately set up, the pulse from the gel-skin interface aligned precisely at the left edge of the screen graticle. The other pulses appear approximately as tall as this pulse, as shown in Figure 3. When the system was properly adjusted, and a measurement was to be made, a special foot petal and circuit was designed to signal the oscilloscope, causing the trace to be stored. A permanent record was made with a Polaroid camera attached to the face of the oscilloscope.

THE INITIAL TESTING OF THE INSTRUMENT

The initial tests were conducted on skin burns on anesthetized pigs. A surgeon scald-burned a small region on the skin, made an ultrasonic measurement, and excised a portion of the burn region for histological study, under the direction of Dr. Robert Diegelmann at MCV. The results were encouraging, but the surgeon had considerable trouble in maintaining perpendicularity of the transducer to the skin surface, a necessary condition to obtaining good reflections from the burn site. A special cylindrical column made of lucite that could be filled with gel was built. When used with the transducers, it placed the surface of the skin at the optimum location and alignment to obtain the best traces. We also began to use slightly lower frequency transducers that were focused, thus making perpendicularity less critical.

After arrangements were made, we established a team of NASA personnel to take measurements on three patients who had been admitted to the burns unit at The Medical College of Virginia (MCV). The procedure was under the supervision of Dr. B. W. Haynes, director of the burns center at MCV, and his staff. Dr. Haynes provided diagnoses, against which we could compare our measurements. In every case, our measurements were in agreement with his diagnoses, both of which were subsequently confirmed by the healing process. We felt that the concept was proven to be useful in the clinical setting, and the instrument and concept were ready to extend to the manufacturer.

THE TRANSFER OF THE TECHNOLOGY

The test site again provided valuable assistance during this phase of the project. For example, Dr. A. Marmarou of MCV critiqued the prototype that we used, and made a number of valuable suggestions. One suggestion included the conversion of the system to a scanning device, enabling the surgeon to obtain an ultrasonic cross-sectional view (B-scan) of significant regions of a burn site.

With help from Mr. John Samos and Dr. Franklin Farmer of our Technology Utilization Office, and in cooperation with Dr. Harold W. Adams from Langley's Office of Chief Counsel, Westminster Medical International Corporation was identified as the firm to refine, build, and market an instrument for burns depth measurement. During the time interval of this study, they had developed a high frequency B-scan ultrasonic instrument, which they interfaced to a personal computer for display and data analysis. Working closely with MCV staff and NASA Langley Research Center, the company has made further refinements in the transducer scanner design, data analysis algorithms, etc., in an effort to develop an market a user-friendly instrument for the measurement of burn wound depth. Details of the instrument are available from the company, whose address is 9 Ramland Road, Orangeburg, NY 10962. Their telephone number is (914) 365-2854.

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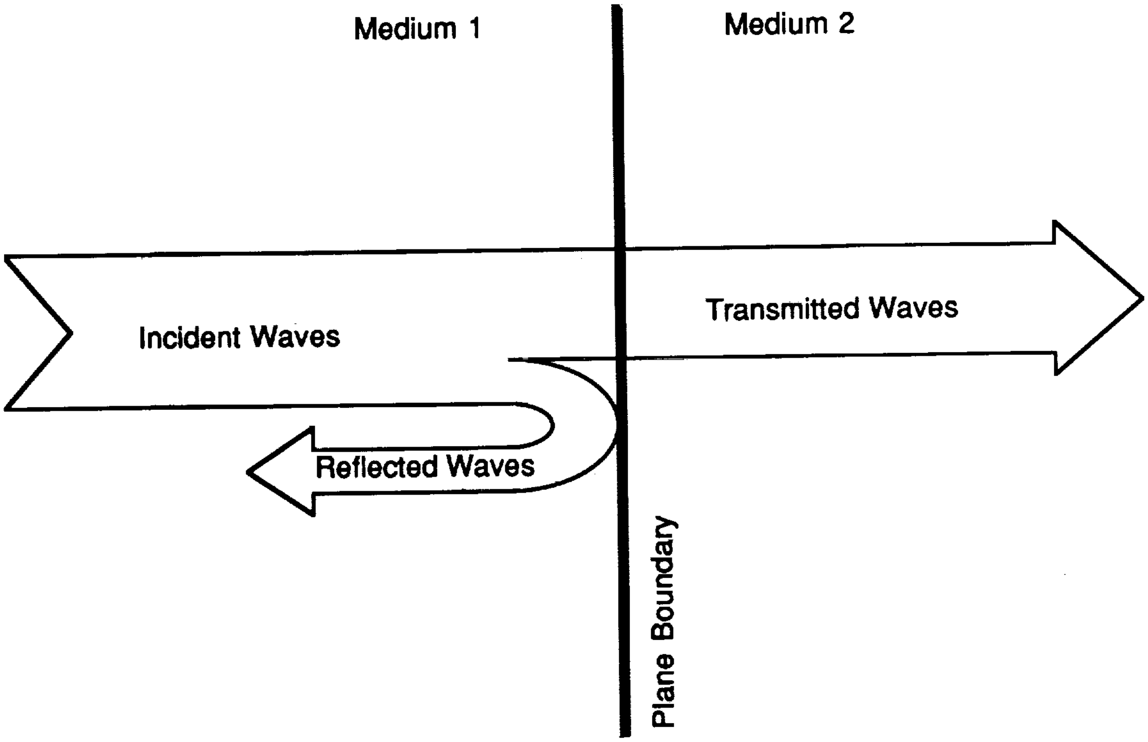

Figure 1. Reflection and transmission of sound waves incident at a boundary between media of different acoustic impedances

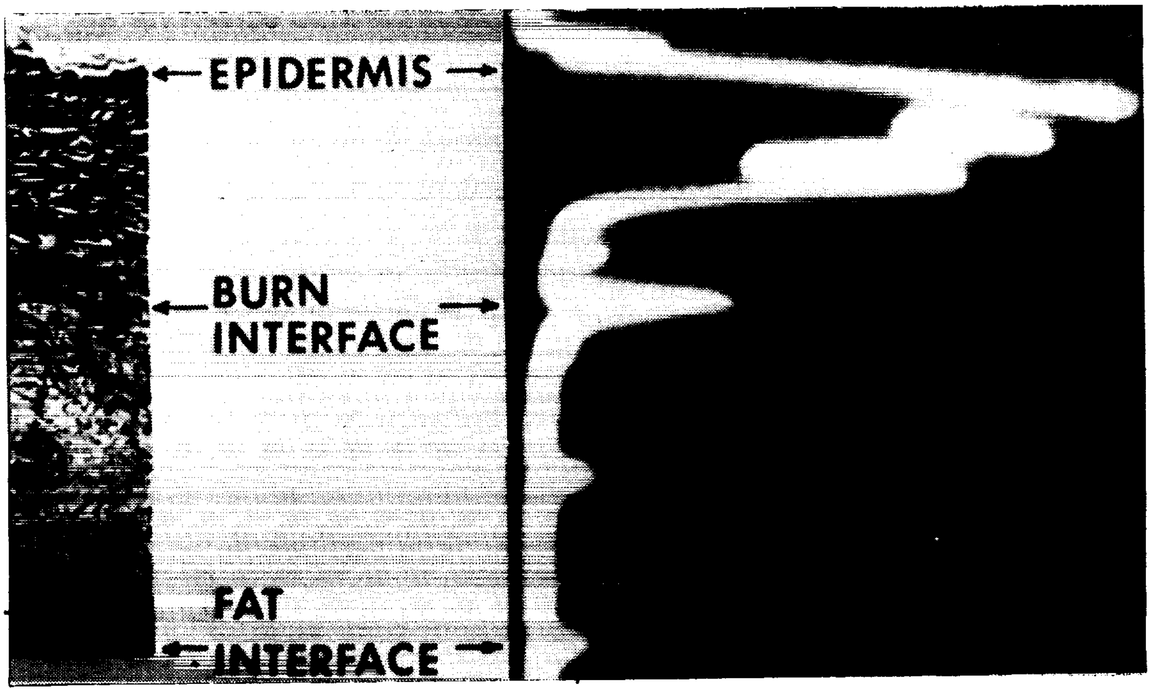

Figure 2. Comparison of a histological section taken immediately postburn with the corresponding ultrasonic pulse-echo data (A-scan trace)

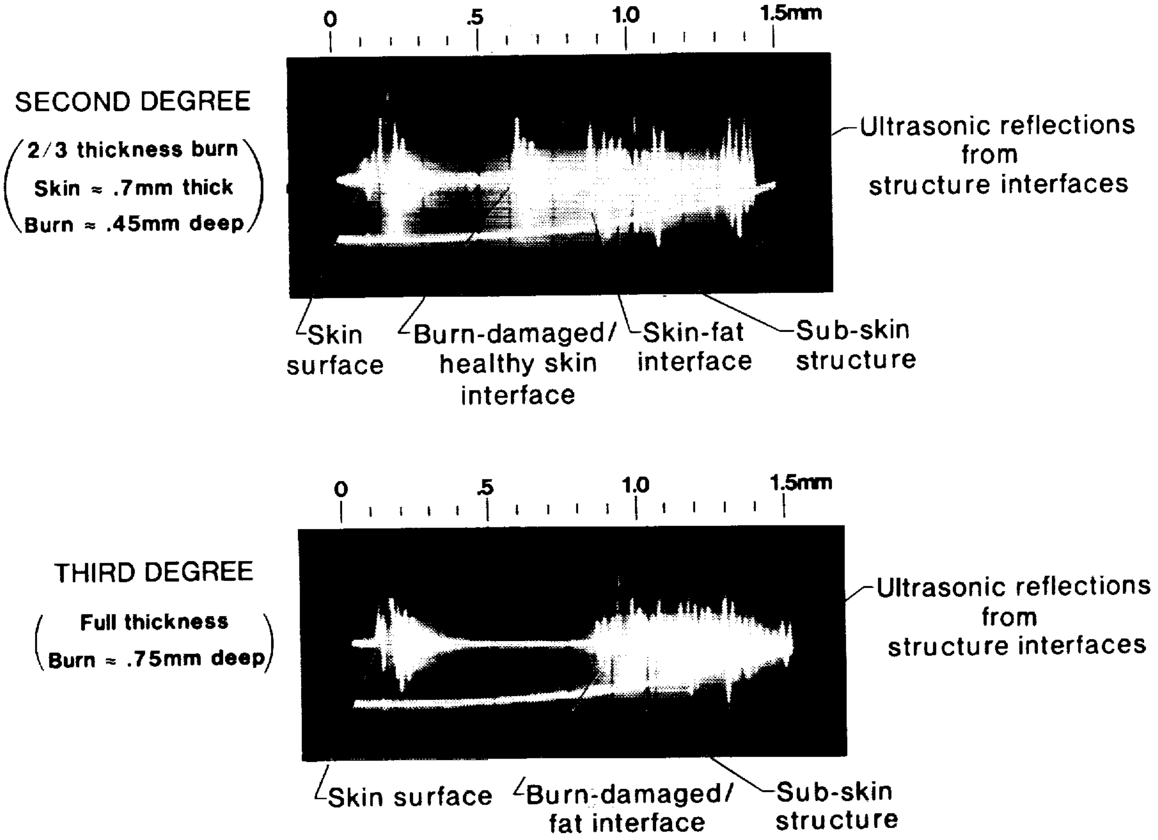

Figure 3. Display ultrasonic pulse-echo data (top trace) of second degree burn injury (dermal, deep dermal) and third degree burn injury (full thickness) in humans, with echos labeled. The bottom trace is the TGC control voltage.