Clinical experiences with ultrasonometric measurement of fracture healing

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Abstract. Introduction: The use of noninvasive, acoustic methods like ultrasonometry is becoming increasingly interesting in the quantitative assessment of fracture healing. A reliable measurement technique has been described using ultrasonic transducers placed across the fracture gap. Ultrasonic image aiming is useful for accurate transducers location, on both sides of the gap. The study was designed to assess the clinical application of measurement of ultrasonic wave propagation through the fracture callus.

Material and Methods: Contact testing was performed with a prototype ultrasonic bone tester UTTK-01 device. The measuring technique was validated experimentally on human long bones in vitro, as well on volunteers. Twenty four diaphyseal fractures of long bones were prospectively assessed. Transducers put on a fixed distance frame were properly placed with ultrasonographic focusing.

Results: Average ultrasound propagation time was 1917 m/s. The measured values for fractures rose with time after injury. The average speed of sound measured between 10\textsuperscript{th} and 21\textsuperscript{st} day after fracture was 1200.85 m/s, after 7 to 8 weeks – 1559.35 m/s, after 12 weeks – 1640.64 m/s, after 16 weeks – 1735.72 m/s.

Conclusions: We conclude that the technique for measuring long bone ultrasound velocity with ultrasonographic centering on the fracture gap allows repetitive positioning of ultrasonic transducers for measurement. Ultrasonic measurement of bone union may support or modify clinical decision. However, further studies are required to make the ultrasonometric method easier and more user friendly for clinical studies.

Keywords: Fracture healing, assessment, monitoring, cortical bone, quantitative ultrasound, ultrasonometry

1. Introduction

Monitoring of fracture healing in clinical practice remains very traditional because of the use of subjective manual manipulation of the fracture site and evaluation of radiographic images in most cases [8,17,47,74,100,103]. Traditional manual testing should determine the quality of bone stiffness of the fracture site. Clinical evaluation is enhanced by X-rays to identify the amount of bridging callus formed [8,37,41,42,48,60,94,100,104]. The majority of subjective fracture healing evaluation methods may lead to some disparity between assessments made by different clinicians of the same patient [17, 74,100,103]. Subjective physical examination of bone union may not lead to correct conclusions, so an assessment using a more objective method of analyzing the degree of healing of a fracture is required for the identification of the completion of fracture healing, and treatment discontinuation.

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Is then quantitative measurement required for fracture healing evaluation? This question still remains open. Until recently we did not have perfect and quantitative definitions of union, delayed union, nonunion or pseudoarthroses. Having definite measurements an orthopedic trauma surgeon would be able to predict refractures, monitor healing processes, set an exact date for the end of immobilization, fixation removal and finally estimate when a patient would be able to return to his/her social life. Realistic and quantitative evaluation of fracture healing may create a new era for orthopedic trauma science. Early detection of delayed union as well as the influence of various factors on fracture healing require an objective method of monitoring. This would provide quantitative assessment of the fracture healing progress. The analysis of how various factors influence fracture healing may be evaluated with precise quantitative measurements of the healing quality and duration. Those factors influencing fracture healing to be tested include biological, pharmacological, physical, mechanical, genetic and others [12,26,44,100].

In general, histology is considered an excellent evaluation method however as an invasive method it may not be applicable in most clinical cases. A reliable method should allow the determination time of adequate union by its strength, quality and quantity. Many non-invasive quantitative techniques for measuring fracture healing have been reported over the past decade, however their acceptance and regular use is rare.

Various methods had been described including: strain gauge instrumentation of fixation devices [24,72], auscultatory percussion [55,61], vibrational analysis [20,29,68], acoustic emission [45,102], absorptiometric techniques [15,28,95,96], ultrasound imaging [11,14,38,53,62,64,80,83], ultrasonometry (quantitative ultrasound) [1,4,9,21,27,30–36,39,40,43,49,56–58,76,78,85,88,89,93,98], resonant methods [10,18,19,70,84,90], impulse response [66,67], spectral analysis [25] and scintigraphy [6,91,101]. These methods usually address direct or indirect stiffness measurements or other features of fracture callus [22,24,97]. Assessment of the bone by steady state analysis utilizes bone response to forced harmonic vibration that relies on natural frequencies which in turn are a function of stiffness and mass [2,22]. Unfortunately, the practical application of vibration methods are limited. Mechanical testing is able to measure stiffness pattern of healing in indirect and direct way [3,16,65,75,81,82] with either invasive or noninvasive procedures. Fractures treated with an external fixator were evaluated using strain gauges on the external fixator [24,65,71], however the accuracy of measurement decreases with pin loosening. A measurement of direct stiffness is typically measured after 6–8 weeks. The tibial fractures were often evaluated. Measurement is performed by angulation at the fracture site quantifying clinical assessment of bone union utilizing X-rays [42,100], or surface measurements after using four point bending. If the value of the stiffness reached 7 Nm/degree (°) no fractures failed to heal after 20 weeks. The radiogram can show some evidence of bone healing indicated by calcification at the callus and fracture gap [41,42,60,94]. However, inaccuracy of x-ray image may lead to the early or too late removal of a fixation device and delay rehabilitation. Direct observation of X-ray image can show callus formation. Simple correlation of callus image and stage of union were often described as poor, however it depends on the experience of the radiologist or surgeon and may be greatly improved with digital enhancement [8,37,42,47,48,94,104]. Accurate measurement of angulation is available for external fixation but is not applicable to internally fixed fractures. The stiffness value of 15 Nm/° of tibial fractures in the anterior–posterior plane in patients treated with external fixators denotes healing. The method is simple to use in the clinical setting and accurate (total error of 3%). Vibrational analysis as a sound wave propagation was described by Lippman in 1932 for fracture healing assessment by percussion proximally and auscultation distally [55]. An impulse response of the bone is assessed by a briefly applied force of a free vibration movement. This method was described [66,67] as a measure of the response to impact using
a crystal transducer. Progress was monitored using the ratio of acceleration between the fractured limb and uninjured limb. This technique has been used to monitor healing tibial fractures in a clinical setting, but requires further validation. Ultrasound velocity measurement in situ predicts the material properties of cortical or cancellous bone and seems to be sufficiently reliable in clinical bone research [7, 9, 13, 21, 27, 30, 32, 39, 40, 49–54, 57, 58, 69, 73, 77–79, 87, 92, 98, 99]. Ultrasound propagation velocity is related to the material properties of bone tissue. In an isotropic material the fundamental equation for ultrasound velocity ($v_{us}$) is:

$$v_{us} = \sqrt{\frac{E}{\rho}}$$

The cortical bone is not isotropic, so the formula may only serve as an approximation. The square root of the materials elasticity and the inverse of the square root of the density determine ultrasound velocity measured along the bone. Measurement of ultrasound wave propagation through the fracture gap is proportional to the stiffness. When ultrasound reflects bone stiffness, then real bone density may be calculated accordingly to fundamental physical equations (wave impedance difference phenomenon $\Delta Z = \rho C = \rho E$, where $E$ – stiffness modulus (Young’s modulus) and $\rho$ – tissue density). This calculation is not possible for bone density measured in g/cm$^2$. Some authors have pointed out problems with soft tissues influencing results but others have neglected errors due to soft tissues and complex bone shapes. The first investigations of ultrasound velocity measurement across a fracture gap were undertaken by Siegel et al. [87] in 1958. Similar experiments were conducted by Abendschein et al., and Gerlanc et al. [1, 32]. The introduction of the SoundScan 2000 [Myriad Ultrasound Systems Ltd, Israel], specifically designed to measure ultrasound velocity along the tibial shaft, overcomes some of these previous measurements errors [30, 52, 73]. However, the SoundScan machine was designed for use in osteoporosis assessment, where the bone remains intact. It was, however, used to investigate whether the SoundScan 2000 might be used for monitoring fracture healing.

Another widely used implementation of ultrasound for examination of the musculoskeletal system is imaging. Ultrasonography was used to estimate the fracture healing progress. Moed and co-investigators proposed an algorithm of standard procedure for early detection of delayed union in patients with tibial fractures treated with locked intramedullary rods [62–64]. Usage of linear probe frequency 7.5 MHz or higher is recommended. The echogenic features of soft tissues neighboring fractured bone are compared to tissues around and inside the fracture gap [38, 62–64]. When the fracture is fixed with intramedullary rod and the remaining fracture gap is open for ultrasound the reflection shadows from implant appear in the gap. Those hyperechogenic signs may disappear after 10 weeks from injury along with callus maturation. The ultrasonic image is still not suitable for measurement of fracture healing progress, it was, however, used to observe and estimate it. In earlier studies we have found that ultrasonic imaging is very useful for ultrasonic transmitter and receiver positioning around the fracture gap [34–36, 38, 40] (see Fig. 1). The economic aspect of ultrasonometric measurement also plays an important role, because a portable device is relatively inexpensive when based on nondestructive testing machine. Finally, the safety of ultrasonic devices is optimal because it utilizes no ionizing radiation or no high magnetic field. This study was designed to assess the clinical application of the measurement of ultrasonic wave propagation through the fracture callus.

2. Material and method

Contact testing was performed with the prototype ultrasonic bone tester UTTK-01 device. The method and investigation plan were accepted by the Bioethical Board of the Medical University. The ultrasonic
bone tester UTTK-01 device produced a signal with an amplitude of approximately 600 V, the electrical energy emitted from the transmitter equals 0.18 mJ per pulse (max. approximately: 0.06 J). The transmitter probe capacity was equal to 1 nF. The energy of ultrasound was estimated as 1/3 of $e$ and depended on the material tested. The testing device has defined impulse emission frequencies from 3 Hz to 1 kHz. Safety of the procedure is high (average power below 0.6 mW). The ultrasonic bone tester (UTTK-01) was supplied with 100 kHz transducers (59 dB, 200 V). Gel for ultrasonography was used to couple the transducers with patient’s skin. The ultrasonic bone tester simply measures the propagation time of ultrasound from transducer to detector and is linked to a PC through a centronix connection.

Measured data were transmitted via PC link and archived. Detected signals are easily transferable via telemedicine connection. Having devices compatible with the database for international multicenter research of fracture healing becomes a real possibility. UTTK-01 transducers were located on the fixed distance frame. The fixed distance of the examination helps in the calculation of the speed of propagation of ultrasound through the bone along its axis. Otherwise the measurement is possible but requires exact distance determination between transducers. Ultrasound is detected by the receiving transducer, after it has traveled 62 mm. The speed of ultrasound along the bone is calculated. A second measurement in an analogue location on the contralateral side is used to compare the results at the same visit. The measured
value of fractured bone serves for monitoring. The measurement technique was validated experimentally on human long bones in vitro, as well on volunteers. The velocity in the cortical bone of the intact tibia was usually approximately 2000 microseconds⁻¹ on previous studies on volunteers [39].

Twenty four diaphyseal fractures of long bones were prospectively assessed. Evaluated fractures were treated employing various techniques including intramedullary, internal or external fixation or immobilization with plaster of Paris. Transducers put on a fixed distance frame were properly placed with ultrasonographic focusing. Only bones covered with thin layer of soft tissues were exposed to ultrasonic bone testing (tibia, radius and ulna).

An individual approach to data evaluation included additionally other features of fracture healing i.e. physical examination, X-ray view, CT or MRI.

3. Results

Images used for centering ultrasonic probes showed not only the fracture gap but also phases of its mineralization (see Fig. 2). Computer tomography and MRI imaging were useful in verifying fracture healing disturbances (see Fig. 3). Fracture cases were examined utilizing various methods and their results were compared (see Fig. 4). Results stored in image or data files were prepared for telemedicine consultation transfer (see Fig. 5).
The results for the intact long bones shafts are presented in Table 1, the results for all the examined bones are listed in Table 2.

Since the aim of this study was to study the ultrasound velocity, statistical analysis for significant differences between intact and fractured bones was made for parameters with a ultrasound propagation time and related velocity of ultrasound. Differences were statistically significant ($p < 0.001$). The increase in the ultrasound velocity is relatively small but very significant while fracture healing progresses, and is much higher than the measurement reproducibility error (approximately 50 m/s for this method).

The ultrasound velocity was measured in intact bones of contralateral extremities of examined subjects served as control and on both legs of volunteers. Lowest and highest values were used to draw borders for ultrasonometric examinations (see Fig. 5). A curve of average measurement values obtained from fractured bones is presented on graph (see Fig. 6).

In a few, normal fracture union cases of who were examined late, after complete remodelling, results showed slightly higher values than those measured on contralateral intact bone (i.e. over one year post fracture). Those late observations may be explained by the presence of well developed and totally remodeled periosteal and endosteal callus. In a few cases of delayed union and pseudoarthroses, measured values stacked with no progress over the time. The transmission of ultrasound may present low measured values and do not reveal significant differences of speed of sound in nonunion cases. The interpretation of the results in such cases may not lead to clear conclusions because of nonsignificant difference of measured values.

4. Discussion

The diagnosis of accurate fracture healing or delayed union or non-union in typical conditions of a busy orthopedic trauma outpatient office can only be made on the basis of the absence of specific changes such as callus formation. Standard X-ray techniques and clinical methods used to follow up the fracture
Ultrasonometric measurement for fracture healing monitoring

Fig. 6. Graph presenting ultrasonic measurement average values: 1- 10–21 days; 2- 7–8 weeks; 3- 12 weeks; 4–16 weeks.

The speed of sound is a good indicator of the stiffening of the healing bone, and increases with progress of healing as described in previous studies [1,7,21,27,32,36,53,85,87,93,98].

The measured values of speed of ultrasound vary among patients [39,52,54,57,73,92,99]. The analogue bone of contralateral extremity is used to compare the measured values and indicate the final endpoint value as well. For typical fracture healing duration no significant bone density changes could be detected within contralateral, intact bone [15,96]. Quantitative ultrasonometric techniques are limited to easily accessible long bone shafts superficially located, like ulnae or tibia. This study has its own limitations, for example, the transverse fracture depicted here is an over simplification, because clinically, long bone
Table 1

Ultrasonometry measurements (velocity of ultrasound = m/s) for intact tibia

<table>
<thead>
<tr>
<th>Avg.</th>
<th>Min.</th>
<th>Max.</th>
<th>Std.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2139.48</td>
<td>1289.67</td>
<td>2873.18</td>
<td>483.04</td>
</tr>
</tbody>
</table>

Table 2

Ultrasonometric values for all measurements

<table>
<thead>
<tr>
<th>Time of US propagation (μs)</th>
<th>(velocity of ultrasound = m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVG 32.33</td>
<td>1917</td>
</tr>
<tr>
<td>Min 17.94</td>
<td>2894.49</td>
</tr>
<tr>
<td>Max 51.63</td>
<td>1200</td>
</tr>
<tr>
<td>Std 8.27</td>
<td>749</td>
</tr>
</tbody>
</table>

Table 3

Average ultrasonometric values of fractured bone in time after fracture

<table>
<thead>
<tr>
<th>Time after injury</th>
<th>Time of US propagation (μs)</th>
<th>(velocity of ultrasound = m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–21 days</td>
<td>51.63</td>
<td>1200.85</td>
</tr>
<tr>
<td>7–8 weeks</td>
<td>39.76</td>
<td>1559.35</td>
</tr>
<tr>
<td>12 weeks</td>
<td>37.79</td>
<td>1640.64</td>
</tr>
<tr>
<td>16 weeks</td>
<td>35.72</td>
<td>1735.72</td>
</tr>
</tbody>
</table>

Fractures are spiral, oblique or comminuted. The velocities of ultrasound measured with our device presents slightly different average values than reported in other studies and taken from tables by Kaye and Laby [46].

Amplitude of ultrasound curve represents attenuation value. The difference between amplitude values of intact and fractured bone reveal the decrease with progress of healing in time and remaining difference if the healing is not progressing.

The UTTK-01 was not designed to measure ultrasound velocity in water bath. Also, the examination may not be performed in such conditions because of the threat of contamination while the fracture is externally fixed with pins passing through the skin.

The measured values of speed of ultrasound vary among patients. The contralateral bone is used to indicate final endpoint value.

Orgee et al. [73] assessed a method for the measurement of ultrasound velocity in cortical bone of the human tibia using a probe designed to minimize the effects of surrounding soft tissues. They found that average maximum velocity gives the lowest errors of reproducibility in relation to the population variance (standardized coefficient of variation = 1.8%). The mid-tibial site was chosen for further studies of bone quality in osteoporosis. The short-term intra- and inter-observer reproducibilities in their study achieved acceptable low values of variation's coefficients 0.35% (n = 22) and 0.50% for the mid-tibial measurements. Unfortunately for measurement’s accuracy fractures rarely appear exactly in mid-tibial region, so that measurements have to be performed in other long bone shaft regions. The contralateral extremity may serve as the control for single measurements or one location is good enough to monitor fracture healing progress in time. For better accuracy, the modification of transducer placement by fracture gap observation on the ultrasonic image with linear 7.5 MHz or higher probe was introduced. The study by Orgee et al. [73] has also shown no significant difference in maximum ultrasound velocity between the dominant and nondominant tibia. Ultrasound transmission velocity measured parallel and
perpendicular to direction of Haversian channels clearly indicated that there is an important influence of architecture in cortical bone on ultrasound transmission velocity which has to be taken into account in its clinical use. Stegman et al. [92] performed a normative population study to achieve data for velocity of ultrasound in tibial cortical bone in a population-based sample of both men and women. Their reproducibility of cortical measurement was found as highly precise (0.5%). The rate of heel and patellar trabecular bone and tibial cortical ultrasound velocity declines with age from the fourth through the ninth decades, being 1.7 m/s per year in men and 4.1 m/s per year in women. They also found that tibial cortical velocity values correlated with patellar velocity and with forearm mineral. No perceptible differences in tibial velocity for patients with or without vertebral fractures were confirmed. They concluded that tibial cortical ultrasound velocity provides useful information about bone status in populations at risk for osteoporosis, and seems particularly well suited for assessing fracture risk of the appendicular skeleton.

Njeh et al. [69] used a tibia phantom to investigate whether the longitudinal propagation velocity of ultrasound across a fracture site could be used quantitatively to assess fracture healing. Using the ultrasound velocity measurement machine SoundScan 2000 they predicted the simulated fracture gap on a phantom with a high degree of accuracy.

Salugozis et al. [85] demonstrated the clinical potential of this technique for the non-invasive assessment of bone fracture healing. They measured the velocity of propagation and attenuation of ultrasound across a fracture gap utilizing 200 kHz transducers. The method shown in their study determined ultrasound velocity and attenuation of longitudinal waves in cortical bone in vivo and in situ on intact and fractured human tibiae. They made an important observation that the measured ultrasound attenuation and velocity were unaffected by the soft tissue between transducers and bone. Their results on intact tibiae of the ultrasound velocity in vivo were $3614 \pm 32$ m s$^{-1}$; $2375 \pm 82$ m s$^{-1}$ on fractured tibiae one week after fracture and $2882 \pm 90$ m s$^{-1}$ on fractured tibiae two weeks later. An attenuation on intact tibiae was $5.52 \pm 0.43$ dB MHz$^{-1}$ cm$^{-1}$, $17.81 \pm 3.91$ dB MHz$^{-1}$ cm$^{-1}$ one week after fracture and $10.42 \pm 3.56$ dB MHz$^{-1}$ cm$^{-1}$ three weeks after injury.

Fellinger et al. [29] augmented standard X-ray techniques to follow up the healing process of bone fractures with a non-invasive method based on evaluation of changes in mechanical vibration reactions. They used a measuring system composed of two sound transducers, an amplifier module and an AD converter attached to a PC. One hundred and fifty healthy individuals were assessed during the initial measuring series and cases after treatment of tibial fractures with an external fixator system. Their study revealed highly significant differences between intact and fractured tibiae. Their studies revealed that computerized sonometry is capable of supplying quantitatively recordable information about the stability of a fractured bone at any time in the healing process and allows early diagnosis of disorders in the repair process by the absence of change in the parameters.

The construction of ultrasonic measuring probes designed for cortical bone assessment has a flat surface which touches skin above the bone. In a fractured bone or while the bone is healing with periosteal callus production, the eminence created by callus may decrease contact of the probe surface with intact bone above and below fracture gap.

If the most important aim is to assess fracture strength, the speed of sound seems to be a good indicator of the stiffening of the healing bone, and increases with progress of healing.

5. Conclusions

Despite the limitations of this study, the results suggest that the combined method consisting of ultrasonometry and ultrasound imaging has potentially better accuracy in quantitative fracture healing.
monitoring. Ultrasonographic images of the fracture gap are helpful for ultrasonometric transducers positioning, centering the fracture gap that allows repetitive position ultrasonic transducers for measurement. A study of healing fracture assessment in vivo using ultrasonometry indicates the value of this method in healing prediction. Ultrasonometry is a reliable and noninvasive method reflecting bone strength but some limitations of the method exist. Ultrasonometry signal may be used for remote analyzing via telemedicine connections. The results of ultrasonometric measurements allow monitoring the progress of bone union quantitatively; however, further studies are required to make this method easier and more user friendly for clinical studies. Further effort is required to develop quantitative methods for monitoring of fracture healing. The progress in fracture healing science is possible not only by development of new treatment devices but also by development of modern scientific tools for Evidence Based Medicine.

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