Can ultrasonographic evaluation of subcutaneous fat predict pressure ulceration?

High-resolution ultrasound may be able to detect pressure ulcers before clinical signs emerge. This retrospective study found that one such early indicator is inflammatory oedema in the subcutaneous fat, whic resolves as healing occurs

ultrasonography; pressure ulcer; fat oedema; deep tissue injury; subcutaneous tissue

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Ultrasonography is an inexpensive, portable and safe technique that does not expose the patient to radiation. As a result, it is widely used in clinical practice. High-resolution ultrasound using a 20MHz probe can detect clear images of the dermis and epidermis, but not the subcutaneous tissue. Dermatological studies using a 20MHz probe have found that ultrasound can be used for the search and imaging of lymph nodes, chronic ulcers and subcutaneous tumours in a variety of clinical settings.[1-3] Studies have also used a 20MHz probe to investigate the effect of pressure ulceration on superficial skin. They found it could show soft-tissue damage and oedema before visible clinical signs emerged.[2,4,5]

A 20MHz probe can only produce images 20mm below the skin surface, making it difficult to detect changes in subcutaneous deep tissue.[3,4] However, it is particularly important to observe this subcutaneous tissue in order to predict deep tissue injury (DTI), which the National Pressure Ulcer Advisory Panel (NPUAP) has defined as a new pressure ulcer (PU) stage.[6,7]

We therefore routinely use a 10MHz probe, which can clearly visualise the dermis, the subcutaneous fatty tissue and muscle 20–30mm below the skin surface. Nagase et al. suggested in a case study that this frequency can be used to observe subcutaneous deep tissues for the early detection of suspected DTI.[8]

Based on our clinical practice, we hypothesise that inflammation or ischaemia caused by pressure ulceration has a greater effect on subcutaneous fat than any other tissue. We believe this is because the subcutaneous fat, and the superficial fascia in the fat, play an important role in protecting the muscle and bone from external forces. We propose that an inflammatory oedema occurs in the subcutaneous fat in the early stages of pressure ulceration, and that excessive tissue damage induced by full-thickness PUs causes necrosis in this layer of tissue. It is possible that ultrasound can depict these changes.

Few reports have analysed the effect of PUs on the subcutaneous tissue. This retrospective study therefore used high-resolution ultrasound images to compare subcutaneous tissue in:

- Ulcerated and non-ulcerated skin
- Patients with PUs in various stages in the progression towards healing
- Superficial and full-thickness PUs.

We hope this will provide data to inform the development of a standardised technique for the use of ultrasound in PU assessment.

Method

Patients and study protocol

We performed a retrospective analysis of the PU database at the University of Tokyo Hospital, Japan. At the hospital, patients with PUs or signs of tissue damage undergo a wound assessment using the DESIGN tool,[9] the PU assessment tool generally used in Japan, and high-resolution ultrasound on a weekly basis. The results of this assessment, including PU severity, are documented and stored on the database.

Patients with at least one PU on the greater trochanter who were admitted to the hospital for more than one week between April and December 2007 were included in this retrospective study.

We selected PUs on the greater trochanter because this allowed for comparison of both the affected and unaffected side on the same patient. Furthermore, they usually have a thicker layer of subcutaneous fat around the bone compared with ulcers on locations such as the sacrum or coccyx. We anticipated this would enables us to observe changes in subcutaneous fat more clearly.

Pressure ulcer depth was assessed using the depth score on the DESIGN tool.[9] The score has five components:

- Persistent redness (d1)
- Lesion extends into dermis (d2)

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- Subcutaneous tissue is affected (D3)
- Muscle, tendon and bone are affected (D4)
- Articular or body cavity is affected (D5).

An upper case 'D' indicates a full-thickness or deep PU and a lower case 'd' represents a lesser severity.

Ultrasound images were used to compare the subcutaneous tissue:

- On the unaffected (contralateral) side with that on the ulcerated side
- Of individual PUs as they progress through the various stages of healing
- Of superficial versus full-thickness PUs. In this investigation, patients with superficial and full-thickness PUs were age and sex-matched.

The study was approved by the ethics committee of the Graduate School of Medicine, University of Tokyo.

Sonographic technique

All ultrasound examinations were performed by specialists in dermatology or plastic surgery with experience of using the technique to assess skin and subcutaneous tissue.

Subjects were examined with the viewpoint in the lateral position. The probe was covered with a film dressing to avoid infection.

The PU or normal skin (contralateral side) surrounding the greater trochanter was scanned using a standardised scanning technique. Sonographic examinations lasted for approximately five minutes.

The protocol for ultrasound scanning during the PU care-round was well established. It specified the probe placement, ultrasound settings and details relating to the image recording, thereby ensuring that images were consistent. Gain control (brightness) and image depth were adjusted for each examination.

Linear-array 10MHz transducers (LOGIQ Book XP, GE Healthcare, Japan) were used.

In normal tissue, the subcutaneous fat between the superficial fascia and deep fascia is depicted by ultrasound as a series of clearly defined layers (Fig 1). The ultrasound was used to observe whether this layer structure was clear or unclear.

Ultrasound findings of the skin and subcutaneous tissues for the different grades of PUs were visualised as follows. First, ultrasound was used to search for either a thickened layer of subcutaneous fat or a heterogeneous hypoechoic area. We hypothesised that the former is indicative of oedema resulting from inflammation during the early stages of pressure ulceration (fat oedema), and the latter is indicative of necrosis.

Oedema in subcutaneous fat was defined as:

- The presence of a coarse, homogeneous, internal echo
- Thickened fat layer
- Unclear layer structure.

If a hypoechoic area was identified, we observed the ultrasound findings to determine its pathological characteristics. For example, an internal echo is indicative of a haematoma. In this way, we aimed to identify whether a haematoma or abscess was present, or if fluid was draining freely from the area. We then determined which layer (dermis, subcutaneous fat or muscle) these findings related to. This in turn influenced the type of treatment given.

Results

Eleven patients with PUs on the greater trochanter were identified from the database. Results for the different types of investigations are given below.

Normal versus contralateral side

Three patients were included in this comparison:

- A 19-year-old woman with a d1 PU
- A 47-year-old woman with a d1 PU
- A 51-year-old man with a d2 PU.

Ultrasound images showed the presence of oedema in the subcutaneous fat of the ulcerated side in all three patients. An example is given in Fig 2. Furthermore, the images of the ulcerated area showed roughness (a coarse, homogeneous, internal echo) and an unclear layered structure.

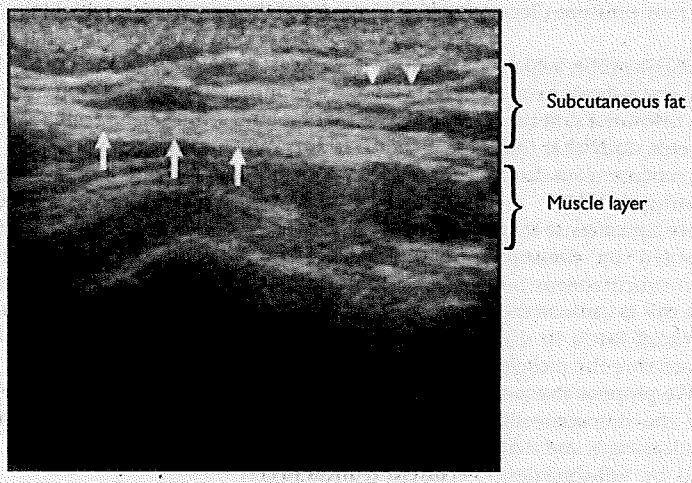
In contrast, the subcutaneous fat on the contralateral side showed no swelling and was clearly observable.

Two patients were discharged after one and four weeks, respectively, when their PUs showed healing trends. The PU of the third patient healed within two weeks.

Pressure ulcers at different stages of healing

Two patients were included in this comparison:

Fig 1. Sonogram of subcutaneous fat, muscle, superficial fascia (arrowheads) and deep fascia (arrows)



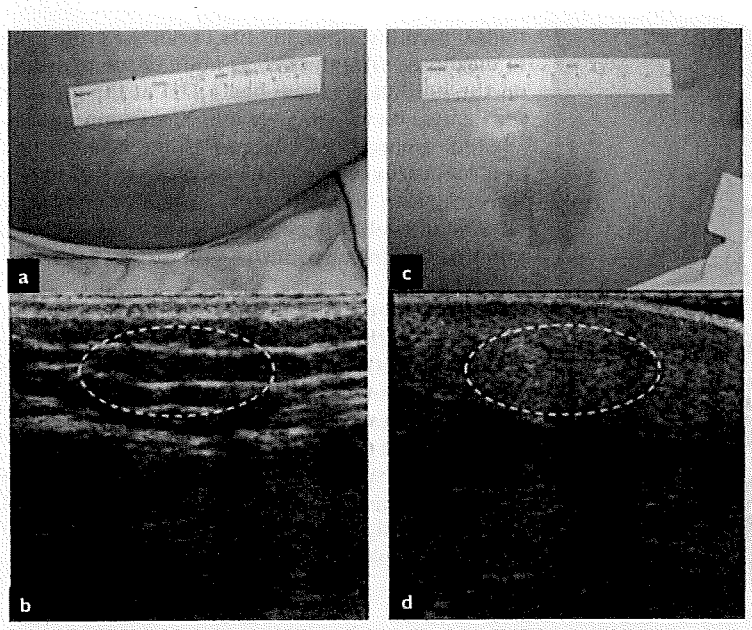


Fig 2. Comparison of ultrasound images of normal (contralateral) and ulcerated tissue in a 19-year-old woman. This pressure ulcer has almost healed (a); ultrasound image of this pressure ulcer, showing a clear layer structure for the subcutaneous fat (b); a d1 pressure ulcer (c); ultrasound image showing fat oedema, with an unclear layered structure for the subcutaneous fat

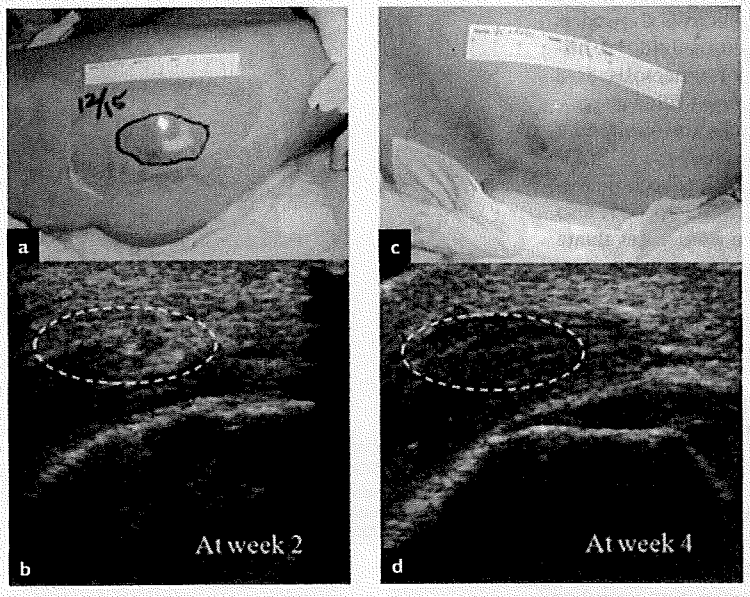


Fig 3. Comparison of ultrasound images of the subcutaneous fat in the various stages of healing of PU in a 67-year-old man: a d1 pressure ulcer at week 2 (a); ultrasound image of this wound (b); the same wound at week 4; ultrasound image showing the reduction in fat oedema

- A 67-year-old man with a d1 PU at weeks 1 and 4
- A 51-year-old man with a d2 PU at weeks 2, 5 and 11.

Initially, fat oedema presented as a thicker fat layer, with an unclear layer structure, in both patients. However, as the wounds improved, subsequent images showed reduced fat oedema and a clearer layer structure. An example is given in Fig 3.

Superficial versus full-thickness PUs

Six patients were included in this comparison:

- A 68-year-old man and an 81-year-old man, both with a D4 PU, and a 74-year-old man with a D5 PU
- A 70-year-old man and a 78-year-old man, both with a d2 PU, and a 67-year-old man with a d1 PU.

Heterogeneous hypoechoic areas in the subcutaneous fat were only identified in the three patients with full-thickness PUs (Fig 4).

Fat oedema was detected for all PUs, regardless of wound depth.

One of the patients with a full-thickness PU died of non-related causes after two weeks. The two remaining patients were discharged after one and two weeks, respectively, with an unchanged wound status.

Two of the patients with superficial PUs were discharged after one week. The third patient healed after two weeks.

Discussion

We hypothesised that oedema is present in the subcutaneous fat in the early stages of pressure ulceration. The ultrasound images showed signs of oedema in the subcutaneous fat of all the PUs. In the images, the superficial fascia in the subcutaneous fat disappeared and the layer structure became unclear as a result of the oedema. These results support our hypothesis.

The ultrasound images of superficial PUs as they progressed towards healing showed that, as the inflammation improved, the layer structure became clearer, indicating that the change in the subcutaneous fat layer is reversible. This is partly because inflammation increases vascular permeability, resulting in oedema during the early stages of pressure ulceration. The inflammation, however, reduces in the later stages of wound healing.[10]

Quintavalle et al.[4] reported that ultrasound visualised oedema in the deep tissue between the bone and skin before clinical signs of ulceration emerged. However, they did not specify which subcutaneous tissue layer was affected. In our study, we have assumed that the subcutaneous fat was visualised as 'fat oedema' as a result of inflammation.

We also hypothesised that excessive tissue damage induced by full-thickness PUs causes fat necrosis. According to our results, full-thickness PUs showed heterogeneous hypoechoic areas in the subcutaneous fat layer.

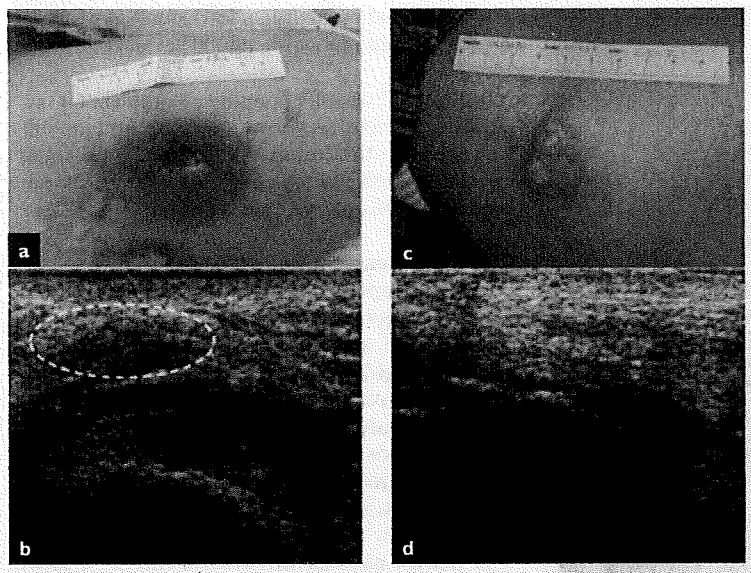


Fig 4. Comparison of ultrasound images of a superficial and full-thickness pressure ulcers: a D4 full-thickness pressure ulcer in an 81-year-old man (a); ultrasound image of this wound showing heterogeneous hypoechoic areas in the muscle layer (b); a d1 superficial pressure ulcer in a 67-year-old man (c); ultrasound showed no signs of a heterogeneous hypoechoic area in this pressure ulcer

Ultrasound is usually able to identify fat necrosis as tissue containing multiple fat lobules.[11] Soo et al. described one of the ultrasound features of subcutaneous fat necrosis as internal echogenic bands.[12] Fernando et al. reported that fat necrosis showed as hypoechoic lobules containing serous fluid.[13] A histopathological study recognised fat necrosis as a sterile inflammatory process with fat-filled macrophages and foreign-body giant cells surrounded by interstitial infiltration of plasma cells.[14]

This suggests that heterogeneous hypoechoic areas are 'fat-fluid' and result from fat necrosis. It also indicates that ultrasound can be used to evaluate areas of fat necrosis in the subcutaneous fat.

While fat oedema caused by a superficial pressure ulceration is reversible, the heterogeneous hypoechoic areas associated with full-thickness PUs appear to be irreversible.

These results suggest that ultrasound is an effective technique for the early detection of PUs, and can also predict their deterioration. It is possible, therefore, that ultrasound can be used to detect fat oedema resulting from damage to soft tissue before visible signs emerge. The fact that ultrasound is an inexpensive, non-invasive imaging modality that produces rapid results would make it an useful and practical tool for diagnosis and follow-up.[8] However, this would require a standardised approach for ultrasound scanning.[15]

This retrospective study does have some limitations. Recently, ultrasound has been used primarily to diagnose DTI. However, as none of the patients on the hospital database had a DTI at the greater trochanter, it was not possible to perform sonographic comparisons between DTI and other types of PUs. Also, as none of the patients were malnourished, it was not possible to determine whether ultrasound could not provide sufficient diagnostic information in patients with a thin layer of subcutaneous fat.

A key study limitation is that it was not possible to obtain histopathological evidence of a PU. In addition, the quality of the images was limited by the portable ultrasound equipment used. Future studies would need to use better quality ultrasound equipment to ensure more effective image evaluation.

Due to the small sample size and the retrospective nature of this study, a prospective, longitudinal study is needed to support our findings before they can be incorporated widely into clinical practice.

Conclusion

This small retrospective study used a 10MHz ultrasound probe to investigate the effect of pressure ulceration on subcutaneous fat. The ultrasound images showed that all of the PUs had signs of inflammatory oedema, which resolved as the wounds healed. In contrast, the fat necrosis associated with full-thickness PUs is irreversible. ■

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Ultrasound Assessment of Deep Tissue Injury in Pressure Ulcers: Possible Prediction of Pressure Ulcer Progression

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Background: The concept of deep tissue injury under intact skin helps us understand the pathogenesis of pressure ulcers, but the best method for detecting and evaluating deep tissue injury remains to be established.
Methods: Intermediate-frequency (10-MHz) ultrasonography was performed to evaluate deep tissue injury. The authors analyzed 12 patients (nine male patients and three female patients aged 16 to 92 years) who showed deep tissue injury–related abnormal findings on ultrasonography at the first examination and were followed up until the pressure ulcer reached a final stage.
Results: The stage of ulcer worsened in six of 12 cases compared with baseline, and healed in the remaining six patients. The authors recognized four types of abnormal signs unique to deep tissue damage in ultrasonography: unclear layered structure, hypoechoic lesion, discontinuous fascia, and heterogeneous hypoechoic area. Unclear layered structure, hypoechoic lesion, discontinuous fascia, and heterogeneous hypoechoic area were detected at the first examination in 12, 10, seven, and five patients, respectively. Unclear layered structure and hypoechoic lesion were more commonly seen in pressure ulcers in deep tissue injury than the other features, but the follow-up study suggested that discontinuous fascia and heterogeneous hypoechoic area are more reliable predictors of future progression of pressure ulcers.
Conclusions: The use of intermediate-frequency ultrasound reliably identified deep tissue injury and was believed to contribute to prevention and treatment of pressure-related ulcers. The results suggest that specific ultrasonographic characteristics may predict which pressure ulcers will progress. (*Plast. Reconstr. Surg.* 124: 540, 2009.)

We sometimes encounter severe deterioration of pressure ulcers initially diagnosed as stage I by visual inspection, and there are some data showing that 10 percent of stage I ulcers and 12 percent of stage II ulcers progress to stage III and IV ulcers despite appropriate care.[1] These are frequently associated with deep tissue damage and are called pressure-related deep tissue injury under intact skin.[2,3] A growing body of evidence suggests that most pressure ulcers are the result of deep tissue injury (bottom-up theory),[4,5] although there may not be sufficient consensus, and further studies are needed.

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Although there are currently several pressure ulcer classifications, such as those by Shea,[6] the National Pressure Ulcer Advisory Panel,[7] and the Japanese Society of Pressure Ulcers,[8] the depth of pressure ulcers and damage to deep tissue are classified only by visual inspection.[1,4] In 2001, the National Pressure Ulcer Advisory Panel concluded that dark purple or bruised areas over bony prominences with intact skin may indicate deeper tissue damage,[9] and the new classifications "suspected deep tissue injury" and "unstageable" were added in 2007.[7] Suspected deep tissue injury was defined as "localized purple or maroon area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by

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tissue that is painful, firm, mushy, boggy, warmer or cooler as compared with adjacent tissue." Although this categorization provides a good approach for evaluating damage to subcutaneous tissue not only by visual inspection but also by palpation and inquiry, we cannot confirm deep tissue injury without using other inspection methods.

The importance of diagnosing deep tissue injury in the early stages and evaluating the prognosis of the pressure ulcer is being recognized. If clinicians can examine subcutaneous tissue, intensive care can be taken at an early stage to avoid further development of pressure ulcers with deep tissue injury. If there is deep tissue injury at admission, later skin deterioration may lead to a possible misunderstanding of the pressure ulcer pathogenesis by the patient and their family; thus, early detection of deep tissue injury is of great value in this sense too. Attempts to detect subcutaneous damage by computed tomography,[10,11] magnetic resonance imaging,[12,13] and ultrasonography have been reported.[10,14–19] Among them, ultrasonography is a safe, economical, noninvasive method and can be easily and repeatedly performed at the bedside. However, there have been few reports and scarce information on the characteristic ultrasonic findings of deep tissue injury and the relationship between the ultrasonic findings and clinical manifestations and prognosis of pressure ulcers. We used intermediate-frequency (10-MHz) ultrasonography to evaluate deep tissue damage under pressure ulcers, and analyzed its potential usefulness in diagnosing deep tissue injury at the early stages and predicting the prognosis of pressure ulcers.

PATIENTS AND METHODS

Two hundred forty-two patients with pressure ulcers were seen at the University of Tokyo Hospital between April of 2006 and March of 2007. To prevent a secondary insult to the skin at the site of the pressure ulcer, patients were put on a pressure-relief bed and kept under intensive nursing care that included periodic position changes. The National Pressure Ulcer Advisory Panel stage at the first examination was stage I in 22 patients, stage II in 150 patients, stage III in 21 patients, stage IV in five patients, and unstageable in 44 patients. The stage "unstageable" is defined by the National Pressure Ulcer Advisory Panel as "full thickness tissue loss in which the base of the ulcer is covered by slough and/or eschar in the wound bed." Ultrasonic assessment of the pressure ulcers was performed to detect deep tissue damage in 144 patients (15 patients with stage I, 90 patients with stage II, 21 patients with stage III, three patients with stage IV, and 15 patients with unstageable ulcers). We detected abnormal signs in 82 of the 120 patients with stage I, II, or unstageble ulcers at the first ultrasonic examination. Nineteen of the 82 patients whose first examination was later than 2 weeks after the ulcer onset were excluded. Twelve of the 63 remaining patients were followed up until the pressure ulcer reached the final stage (range of follow-up, 21 to 179 days). In this preliminary study, we analyzed the clinical and ultrasonic findings of the 12 patients (nine male patients and three female patients; age range, 16 to 92 years). Summarized data from the 12 patients are listed in Table 1.

Table 1. Summarized Data for 12 Patients with Ultrasonically Detected Deep Tissue Injury

Patient	Age (yr)	Sex	Location	Primary Disease	Cause	Primary Stage (NPUAP)	Primary Size (cm)
1	21	F	Right greater trochanter	Acute drug intoxication	Loss of consciousness	II	17.0 × 5.0
2	81	M	Right greater trochanter	Quadriplegia	Loss of consciousness	Unstageable	5.5 × 3.9
3	81	M	Sacrum	Quadriplegia	Loss of consciousness	Unstageable	6.7 × 4.1
4	47	F	Left greater trochanter	Brain tumor	Prolonged surgery	I	5.5 × 5.5
5	16	M	Sacrum	Cardiomyopathy	Prolonged surgery	I	6.5 × 4.5
6	92	F	Spine	Pneumonia	Loss of consciousness	II	4.0 × 3.0
7	66	M	Sacrum	Hepatocellular carcinoma	Immobilization	II	4.8 × 3.5
8	73	M	Sacrum	Rheumatism	Immobilization	II	9.0 × 7.0
9	73	M	Ischium	Rheumatism	Immobilization	Unstageable	5.0 × 1.5
10	51	M	Right greater trochanter	Dissecting aneurysm	Prolonged surgery	II	8.4 × 4.0
11	66	M	Left greater trochanter	Hepatocellular carcinoma	Immobilization	I	5.0 × 3.5
12	77	M	Sacrum	Prostate cancer	Immobilization	Unstageable	5.3 × 3.8

NPUAP, National Pressure Ulcer Advisory Panel; F, female; M, male.

The patients were checked periodically (almost every week); the grade of pressure ulcer was evaluated with visual inspection according to the National Pressure Ulcer Advisory Panel classification, and the ulcer's appearance and ultrasound images were recorded. We used a portable ultrasound system with a 10-MHz probe (Logic Book XP; GE Healthcare, Chalfont St. Giles, United Kingdom) at the bedside. The ultrasonic images were read and evaluated by three persons (one nonblinded author who knew the clinical ulcer stages and two blinded authors who did not know them). A majority of the evaluated grades was regarded as the outcome for each evaluation.

RESULTS

Through our experience with ultrasonic assessment of pressure ulcers, we recognized four types of ultrasound features (described in detail later) as typical abnormal signs of deep tissue damage. These are unclear layered structure, hypoechoic lesion, discontinuous superficial or deep fascia, and heterogeneous hypoechoic area. Representative images are shown in Figure 1. An unclear layered structure is a subcutaneous condition that does not show a clear, layered structure, such as a subcutaneous fatty layer, superficial fascia, deep fascia, muscular layer, bursa, and bone (periosteum). An unclear layered structure usu-

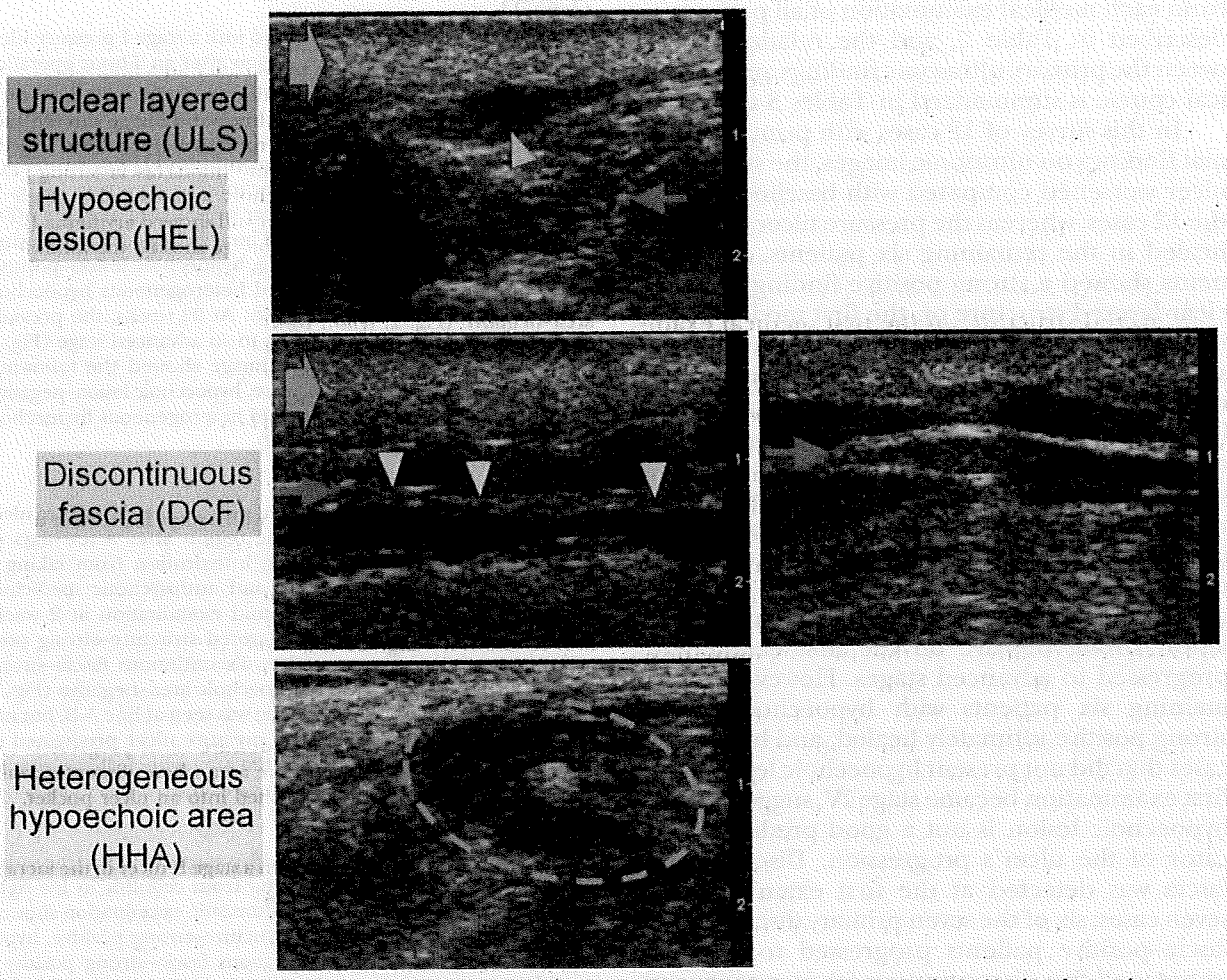

Fig. 1. Representative findings from ultrasonic images specific to deep tissue injury in pressure ulcers. Unclear layered structure (*ULS*) with a coarse echo texture (*violet arrow*) is most frequently seen in pressure ulcers, whereas a hypoechoic lesion (*HEL*) (*blue arrowhead*) is suspected of reflecting a small lesion with fluid, such as seroma and hematoma (*above*). A superficial fascia overlying the muscles is clearly seen as a hyperechoic line on the ultrasound images (*center, right*), whereas discontinuous superficial or deep fascia (*DCF*) (*yellow arrowheads*) shows a broken or discontinuous line with heterogeneous echo signals (*center, left*). A heterogeneous hypoechoic area (*HHA*) is shown by an *orange dashed circle* (*below*). The superficial fascia is indicated with a *red arrow*.

ally has a foggy-appearing area with low contrast and rough resolution. A hypoechoic lesion is a small lesion with a relatively clear margin that has no or little echoic signal and may correspond to a nonvascularized area, such as a hematoma, seroma, or necrotic tissue. A discontinuous fascia is an interrupted high-signal line corresponding to the superficial or deep fascia, which likely means damaged, disrupted, or ruptured fascia. A heterogeneous hypoechoic area is a round or oval area with a heterogeneous internal echo, which disrupts the normally layered structure. A heterogeneous hypoechoic area sometimes has a diffuse border. For each typical ultrasonic abnormal sign, an ultrasonic image was evaluated and classified into three grades: strong positive, positive, and negative. The clinical and ultrasonic evaluations from each medical examination of all patients are described in Table 2, and the relationship between the primary ultrasonic findings and the clinical course is summarized in Tables 3 through 5.

In this survey of 12 cases with primary abnormal findings on ultrasonic images, the stage of the ulcer worsened compared with baseline in six of the 12 cases, whereas the pressure ulcer eventually healed in the remaining six patients. All 12 patients showed a strong positive finding of an unclear layered structure on the first medical examination, suggesting that an unclear layered structure is the most common abnormal finding in ultrasonic examinations (Table 3). The unclear layered structure improved from strong-positive to a better grade within 2 weeks in six patients, in whom all of the pressure ulcers healed. In contrast, in five patients with strong-positive unclear layered structure persisting for more than 2 weeks, the pressure ulcer progressed to an advanced grade (Table 2). Four of 10 cases with hypoechoic lesion–strong positive on the first examination progressed to advanced stages. However, the remaining six patients with hypoechoic lesion–strong positive ultimately healed, and both of two cases that did not present hypoechoic lesion at the first examination became stage IV, suggesting that hypoechoic lesion is not a good predictive indicator of the ulcer's progression. Discontinuous fascia was detected at the first examination in seven cases; six of the seven primary discontinuous fascia–positive patients progressed to stage IV, whereas all five discontinuous fascia–negative patients eventually healed without the ulcer getting worse (Table 3). Six patients who ultimately progressed to stage IV had discontinuous fascia at the first examination. Considered together, discontinuous fascia appears to be a reliable predictor of advancement of ulcer stage, with one false-positive and no false-negative patients. A heterogeneous hypoechoic area was strongly positive in five patients at the first examination, and all five heterogeneous hypoechoic area–strong positive patients ultimately progressed to stage IV. Six of seven heterogeneous hypoechoic area–negative patients healed without getting worse, although one patients with a negative heterogeneous hypoechoic area progressed to an advanced stage. Thus, heterogeneous hypoechoic area also seems to be a good indicator of stage of advancement, with one false-negative patient and no false-positive patients.

CASE REPORTS

Case 1

A 47-year-old woman presented with a stage I pressure ulcer in the left greater trochanter region after an 8-hour operation for brain tumor resection. Induration was palpated subcutaneously (Fig. 2, *above, left*), and the ultrasound image showed the following: unclear layered structure–strong positive, hypoechoic lesion–strong positive, discontinuous fascia–strong positive, and heterogeneous hypoechoic area–negative (Fig. 2, *above, right*). After 1 week, the ulcer still showed erythema (Fig. 2, *center, left*), and the ultrasound image showed the following: unclear layered structure–positive, hypoechoic lesion–positive, discontinuous fascia–positive and heterogeneous hypoechoic area–negative (Fig. 2, *center, right*). At 24 weeks, the pressure ulcer healed without progressing to an advanced stage (Fig. 2, *below, left*), and the ultrasound image showed the following: unclear layered structure–negative, hypoechoic lesion–negative, discontinuous fascia–negative, and heterogeneous hypoechoic area–negative (Fig. 2, *below, right*).

Case 2

A 21-year-old woman presented with a stage II pressure ulcer in the right greater trochanteric region after a few days of immobilization after acute drug intoxication from taking a large quantity of sleeping pills and antipsychotic medicines (Fig. 3, *above, left*). The ultrasound examination at 2 weeks showed the following: unclear layered structure–strong positive, hypoechoic lesion–negative, discontinuous fascia–strong positive, and heterogeneous hypoechoic area–negative (Fig. 3, *right panels*); a discontinuous fascia was seen at line A-B, but not at line C-D. After 11 weeks, the pressure ulcer progressed to stage IV (Fig. 3, *below, left*), and the area where discontinuous fascia was observed at 2 weeks turned into an ulcer pocket.

Case 3

A 73-year-old man presented with a stage II ulcer in the sacral region after septic shock resulting from cellulitis in his right lower leg (Fig. 4, *above, left*). An ultrasonic examination showed the following: unclear layered structure–strong positive, hypoechoic lesion–positive (discontinuous fascia–strong positive), and heterogeneous hypoechoic area–strong positive. A heterogeneous hypoechoic area was seen at line A-B and line C-D (Fig. 4, *above, right* and *center, right*). Two weeks later, the pressure ulcer advanced to unstageable (Fig. 4, *center, left*); both areas with heterogeneous hypoechoic area developed into deep ulcers. At that time, discontinuous fascia and a heterogeneous hypoechoic area were detected at line E-F, which also pro-

Table 2. Staging and Ultrasonic Findings at Each Examination for 12 Patients with Ultrasonically Detected Deep Tissue Injury

Patient	Time Point from First Examination (Time from Onset*)	NPUAP Stage	Ultrasonic Findings			
			Unclear Layered Structure	Hypoechoic Lesion	Discontinuous Fascia	Heterogeneous Hypoechoic Area
1	0 (1W)	II	N/A	N/A	N/A	N/A
	1W	Unstageable	++	−	+	−
	2W	Unstageable	N/A	N/A	N/A	N/A
	4W	Unstageable	N/A	N/A	N/A	N/A
	5W	Unstageable	N/A	N/A	N/A	N/A
	6W	Unstageable	N/A	N/A	N/A	N/A
	7W	Unstageable	N/A	N/A	N/A	N/A
	10W	Unstageable	N/A	N/A	N/A	N/A
	11W	IV	N/A	N/A	N/A	N/A
2	0 (s/2W)	Unstageable	++	++	+	+
	2W	Unstageable	++	++	+	+
	3W	IV	N/A	N/A	N/A	N/A
3	0 (s/2W)	Unstageable	++	++	+	+
	2W	Unstageable	++	++	+	+
	3W	IV	N/A	N/A	N/A	N/A
4	0 (5D)	I	++	++	+	−
	1W	I	+	+	+	−
	25W+4D	Healed	−	−	−	−
5	0 (0D)	I	N/A	N/A	N/A	N/A
	2W	Unstageable	++	++	−	−
	3W	Unstageable	+	+	−	−
	4W	Unstageable	−	−	−	−
	5W	II	−	−	−	−
	11W	Healed	−	−	−	−
6	0 (5D)	II	++	++	−	−
	1W	II	+	+	−	−
	24W	Healed	−	−	−	−
7	0 (s/1W)	II	++	++	−	−
	1W	II	+	+	−	−
	4W	II	++	++	−	−
	5W	II	+	+	−	−
	5W+2D	Healed	N/A	N/A	N/A	N/A
8	0 (s/1W)	II	++	++	+	+
	2W	Unstageable	++	++	+	+
	3W	IV	N/A	N/A	N/A	N/A
9	0 (s/1W)	Unstageable	++	++	+	+
	2W	Unstageable	++	++	+	+
	3W	Unstageable	++	++	+	+
	4W	IV	N/A	N/A	N/A	N/A
10	0 (1D)	II	N/A	N/A	N/A	N/A
	5D	II	++	++	−	−
	1W + 5D	II	+	+	−	−
	2W + 5D	II	+	+	−	−
	3W + 5D	Unstageable	++	+	+	−
	4W + 5D	Unstageable	++	+	+	−
	5W + 5D	Unstageable	+	+	−	−
	6W + 5D	Unstageable	+	+	−	−
	7W + 5D	Unstageable	+	+	−	−
	8W + 5D	IV	+	−	−	−
	9W + 5D	IV	+	−	−	−
	23W	Healed	N/A	N/A	N/A	N/A
11	0 (s/1W)	I	++	++	−	−
	1W	I	++	++	−	−
	2W	I	+	+	−	−
	4W	Healed	−	−	−	−
12	0 (s/2W)	Unstageable	++	−	+	+
	1W	Unstageable	++	−	+	+
	2W	Unstageable	++	−	+	+
	3W	IV	N/A	N/A	N/A	N/A

NPUAP, National Pressure Ulcer Advisory Panel; N/A, not available; ++, strong positive; +, positive; −, negative.
*Values in parentheses (time from onset) represent the exact or suspected time of the first medical examination from the onset of the pressure ulcer (e.g., 10D and s/2W mean exactly 10 days and suspected 2 weeks, respectively). The time point from the first examination is expressed as the "time from the first examination" (e.g., 5W + 4D means 5 weeks 4 days).

Table 3. Summarized Data of the Relationship between Changes in Ulcer Staging and Deep Tissue Injury–Associated Ultrasonic Findings

		Ultrasonic Findings at First Examination			
NPUAP Stage at First Examination	NPUAP Stage at Final Examination	Unclear Layered Structure	Hypoechoic Lesion	Discontinuous Fascia	Heterogeneous Hypoechoic Area
I	Healed	++	++	−	−
I	Healed	++	++	+	−
II	Healed	++	++	−	−
II	Healed	++	++	−	−
II	Healed	++	++	−	−
II	IV	++	++	+	+
Unstageable	Healed	++	++	−	−
Unstageable	IV	++	−	+	−
Unstageable	IV	++	−	+	+
Unstageable	IV	++	++	+	+
Unstageable	IV	++	++	+	+
Unstageable	IV	++	++	+	+
Positive predictive value for ulcer progression		50.0% (6/12)	40.0% (4/10)	85.7% (6/7)	100.0% (5/5)
Specificity for ulcer progression		0.0% (0/6)	0.0% (0/6)	83.3% (5/6)	100.0% (6/6)
Sensitivity for ulcer progression		100.0% (6/6)	66.7% (4/6)	100.0% (6/6)	83.3% (5/6)

NPUAP, National Pressure Ulcer Advisory Panel; N/A, not available; ++, strong positive; +, positive; −, negative.

Table 4. Calculation of Positive Predictive Value, Specificity, and Sensitivity

	Outcome-Positive (Progression)	Outcome-Negative (Healing)
Test-positive	A	B
Test-negative	C	D

Table 5. Positive Predictive Value, Specificity, and Sensitivity of Each Feature for Ulcer Progression Were Calculated According to the Calculating Formula*

Values	Calculating Formula
Positive predictive value (%)	A/(A + B) ×100
Specificity (%)	D/(B + D) ×100
Sensitivity (%)	A/(A + C) ×100

* Positive predictive value is the ratio of both the test-positive (ultrasonic finding) and outcome-positive (ulcer progression) number to the total test-positive number. Specificity is the ratio of both the test- and outcome-negative numbers to the total outcome-negative number. Sensitivity is the ratio of both the test- and outcome-positive number to the total outcome-positive number.

gressed to a stage IV ulcer 1 week later, and the necrotic tissue was removed (Fig. 4, *below, left*).

DISCUSSION

Diagnosis of Deep Tissue Injury with Ultrasonography

Recently, the concept of deep tissue injury under intact skin has helped us understand the pathogenesis of pressure ulcers but has suggested that existing staging systems may not be adequate to classify pressure-related damage of the skin and soft tissue.[1] Diagnosis of deep tissue injury cannot be verified unless methods other than visual inspection are used. Magnetic resonance imaging is not adequate for daily assessments; thus, ultrasonography is expected to become the tool used in practice to examine deeper tissue damage. Several studies have reported results on ultrasonography for pressure ulcers and showed ultrasound images of suspected deep tissue injury, such as edema[16,17] and necrotic tissue,[10,14,19] although the quality of the ultrasound images was not good and detailed information obtained from the images was not fully analyzed.[10,14–18]

Our results suggest the potential usefulness of intermediate-frequency ultrasonography to diagnose deep tissue injury and predict ulcer progression. We believe that an intermediate frequency (10 MHz) is adequate for assessing deep tissue injury, although a higher frequency (>20 MHz) was used for pressure ulcers in previous reports.[16–18] The higher frequency of ultrasonography generally leads to greater resolution of images of the skin and underlying soft tissue,[20] but the visualized depth and range are not deep and wide enough to accurately identify deep tissue injury signs. All the layers, from the subcutaneous adipose tissue to the bone, need to be checked, and findings of the deep fascia and muscle layers are especially critical. Tissue pressure was measured as three to five times higher internally near a bony prominence than at the skin.[21]

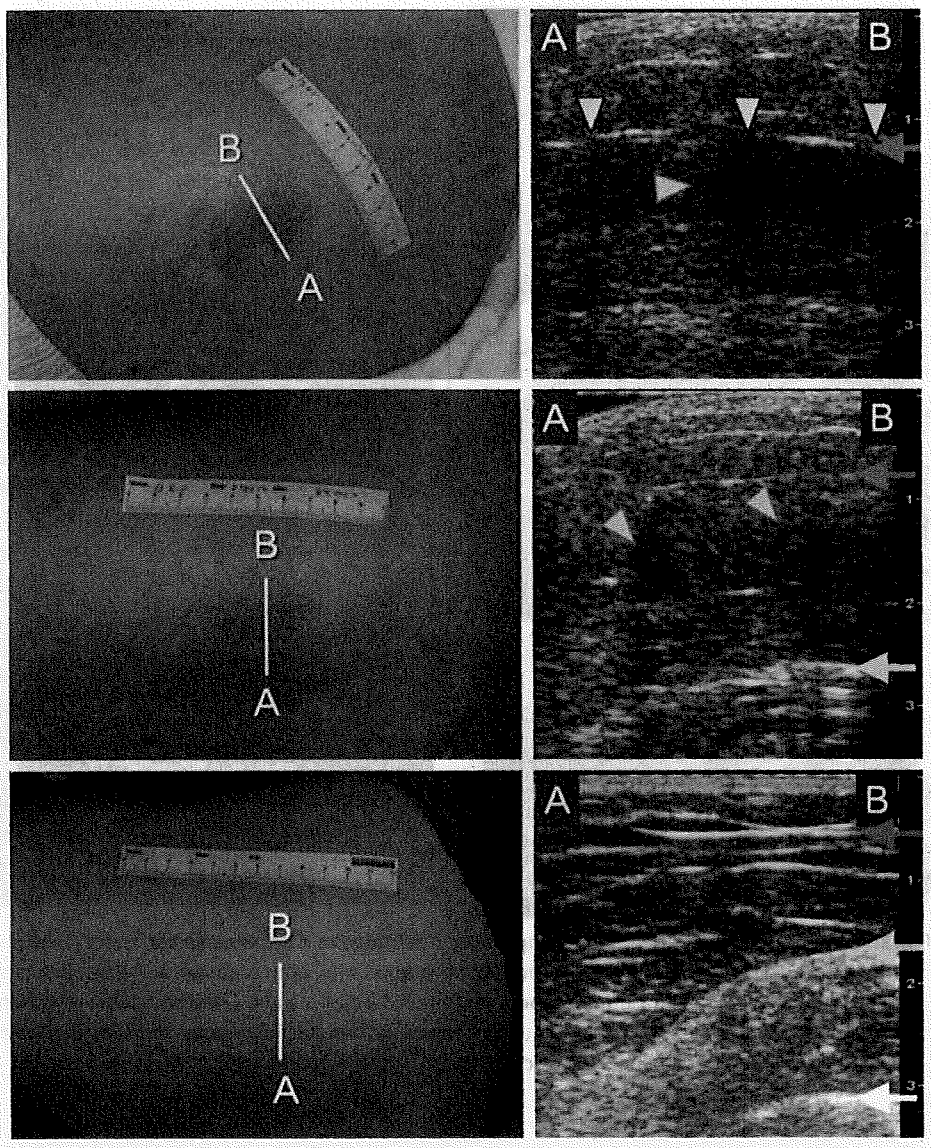

Fig. 2. Case 1 (patient 4 in Table 1). Outer appearance (*left*) and ultrasonographic manifestations (*right*) at baseline (the first examination; *above*), after 1 week (*center*), and after 24 weeks (*below*). Bars on the *left* show where an ultrasound probe was applied. Line *A-B* indicates the direction of the applied probe in the visual (*left*) and ultrasound (*right*) images. *Light blue* and *yellow arrowheads* indicate hypoechoic lesion and discontinuous fascia, respectively. *Red, yellow,* and *white arrows* indicate the superficial fascia, the deep fascia, and the greater trochanteric bursa, respectively.

Characteristic Findings of Deep Tissue Injury on Ultrasonography

Through our experience with ultrasonography for deep tissue injury detection of pressure ulcers, four findings unique to deep tissue damage were recognized: unclear layered structure, hypoechoic lesion, discontinuous fascia, and heterogeneous hypoechoic area. When one of these four features is seen, we may diagnose it as deep tissue injury.

An unclear layered structure was observed in all 12 patients followed and seems to be the ultrasonic sign most commonly seen in deep tissue injury. An unclear layered structure likely reflects subcutaneous tissue damage such as edema, interstitial fluid, and inflammation that result in a coarse echo texture and the unclear margins of each layer in echoic images. An acoustic shadow or dorsal echo extinction arising from inflammation-

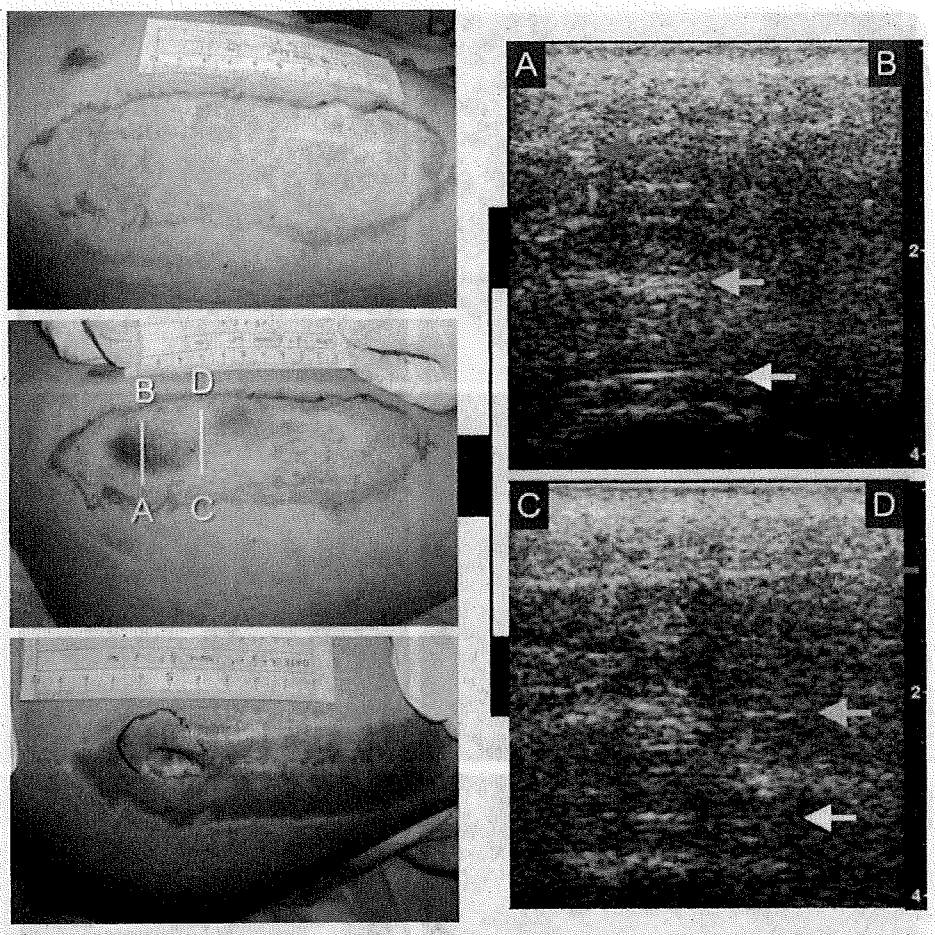

Fig. 3. Case 2 (patient 1 in Table 1). Outer appearances (*left*) (*above*, at baseline; *center*, after 2 weeks; *below*, after 11 weeks) and ultrasonographic manifestations (*right*; both obtained at 2 weeks). Bars on the *left* show where an ultrasound probe was applied. Lines *A-B* and *C-D* indicate the direction of the applied probe in the visual (*left*) and ultrasound (*right*) images. *Red*, *yellow*, and *white arrows* indicate the superficial fascia, the deep fascia, and the greater trochanteric bursa, respectively.

induced hard subcutaneous tissue or induration was occasionally seen, although the causative object remains unclear. An unclear layered structure was detected during the first examination in all cases; half of the 12 patients healed, and ulcers in the other half progressed to stage IV. These results suggest that unclear layered structure is not a specific predictor of ulcer progression but a sensitive indicator of existing deep tissue injury. An unclear layered structure may represent initial subcutaneous reactions, such as edema or inflammation after receiving substantial pressure or shear force. All six of the patients with unclear layered structure that persisted more than 2 weeks had ulcers that progressed to advanced stages, suggesting that persisting unclear layered structure may be used as a predictor of ulcer stage advancement. A hypoechoic lesion was seen at a relatively high rate (83.3 percent) in our study, and a very recent study using 10-MHz ultrasonography for spinal injury patients suggested it as a possible sign of deep tissue injury.[19] However, its positive predictive value, specificity, and sensitivity for ulcer stage progression were unexpectedly low (40, 0, and 66.7 percent, respectively) in this preliminary study with a small sample size (Tables 3 through 5).

The ultrasound image of a discontinuous fascia may be derived from inflammatory changes, ischemia, or anatomical disruption of the superficial or deep fascia. Strong inflammation and edema may cause hyperlucency of the fascia on ultrasound images. In addition, disruption of the vascular network in the deep fascia, resulting in necrosis and lysis of the fascia, likely leads to hy-

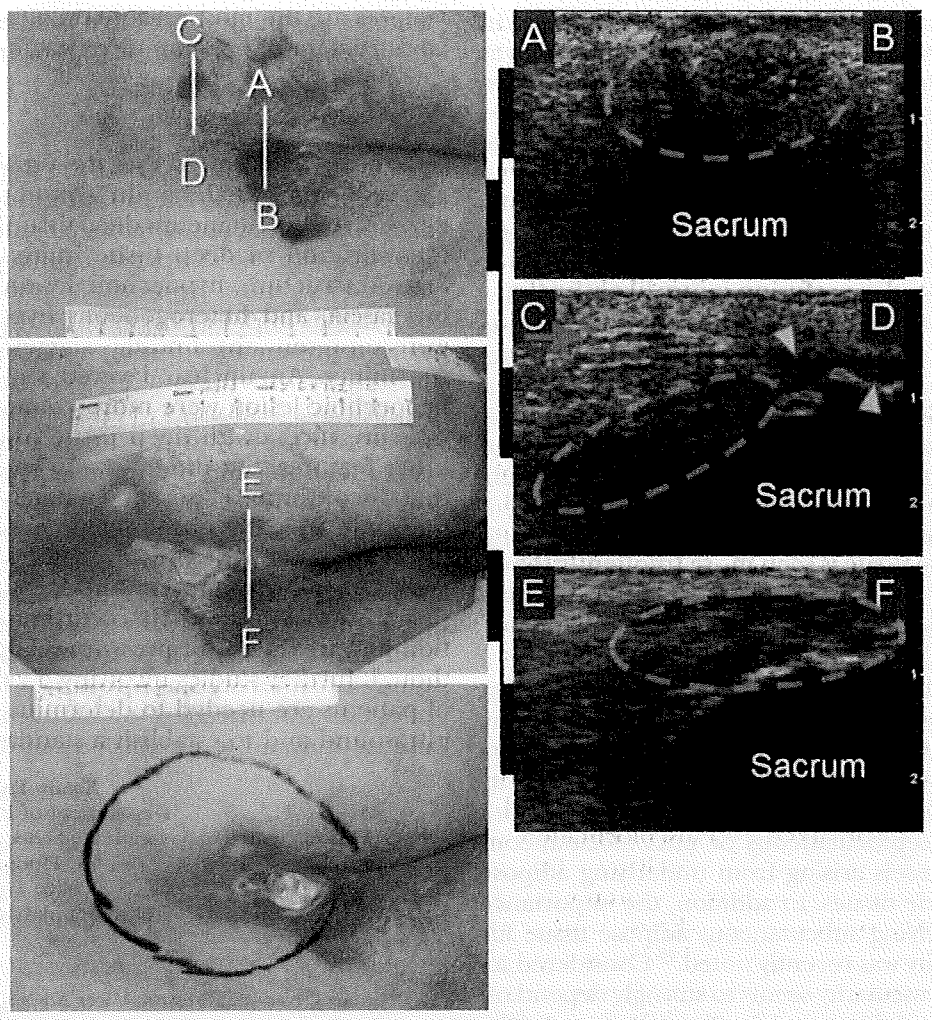

Fig. 4. Case 3 (patient 8 in Table 1). Outer appearances (*left*) (*above*, at baseline; *center*, at 2 weeks; *below*, at 3 weeks) and ultrasonographic manifestations (*right*) (*above* and *center*, at baseline; *below*, at 2 weeks). Bars on the *left* show where an ultrasound probe was applied. Lines *A-B* and *C-D* indicate the direction of the applied probe in the visual (*left*) and ultrasound (*right*) images. *Light blue arrowheads*, *red arrows*, and *orange dashed circle* indicate hypoechoic lesion, the superficial fascia, and heterogeneous hypoechoic area, respectively.

poechoic changes on ultrasonography. The image of a heterogeneous hypoechoic area would represent a necrotic area containing necrotic tissue, debris, and fluid; the necrotic area shows a heterogeneous area on ultrasound, with relatively low internal echo. Our results suggested that discontinuous fascia and heterogeneous hypoechoic area observed during the first examination may predict future deterioration of the pressure ulcer with high probability. Unlike unclear layered structure and hypoechoic lesion, the positive predictive value, specificity, and sensitivity of discontinuous fascia and heterogeneous hypoechoic area for ulcer stage progression was very high (discontinuous fascia, 85.7, 83.3, and 100 percent; and heterogeneous hypoechoic area, 100, 100, and 83.3 percent, respectively). Furthermore, our case reports showed that ulcer pockets formed at the site where discontinuous fascia and/or heterogeneous hypoechoic area were detected.

Potential Mechanisms for Deep Tissue Injury

Deep tissue damage is thought to be induced through two main mechanisms of external and internal pressure forces (and their interaction

with each other), although most superficial skin injuries are related to nonpressure factors, such as friction, maceration, and moisture.[5] External pressure and/or shear force and its counteractive force from bone prominences directly cause tissue ischemia and deformation, leading to deep tissue necrosis.[22,23] In contrast, as in the instances of compartment syndrome, significant swelling can cause ischemia and tissue necrosis.[24] Not only ischemia but also repeated reperfusion injury likely further deteriorates the deep tissue[5]; only 3-hour ischemia followed by reperfusion induced significant irreversible damage to subcutaneous adipose tissue in a mouse model.[25]

It is established that skin has more tolerance to ischemia than subcutaneous tissues such as subcutaneous adipose and muscle tissue.[26–28] Indeed, the lysis or partial necrosis of subcutaneous adipose or muscle tissue is seen more frequently than skin necrosis after free flap transplantation. Because of the differential tolerance to ischemia, deep tissue injury under intact skin would be a rather natural phenomenon that should occur in the early phase of pressure ulcer formation at any site where substantial adipose and/or muscle tissue exists on the bone prominence. The skin vascularity is based not only on the subdermal vascular network but also on septocutaneous or musculocutaneous perforator vessels arising from underlying adipose and/or muscle tissues. In addition, the importance of the underlying subcutaneous adipose tissue for skin vascularity was recently noted.[29] Considered together, skin vascularity seems to strongly depend on the underlying tissues, and severe damage to the deep tissue likely impairs skin viability. Thus, we believe that the bottom-up theory is supported by a huge body of clinical and experimental evidence; external pressure leads to necrosis that first develops in subcutaneous fat and/or muscle tissue and then appears later in the skin.[4,5]

If deep tissue necrosis is within the absorbable limit of size, the necrotized tissues would be replaced with regenerated tissue and/or scar tissue. In contrast, if the necrosis expands to a nonabsorbable size, the pressure ulcer may progress to advanced stages. Although it is speculative to describe the sequence of the four ultrasonic features, unclear layered structure would appear first and prolonged pressure may lead to discontinuous fascia. Heterogeneous hypoechoic area may develop if there is persisting ischemia or if deformation is applied to a hypoechoic lesion. Necrotic changes to deep tissues may be best reflected by discontinuous fascia and a heterogeneous hypoechoic area in our assessment. Our results suggest that both of these features are the most reliable predictors for future advancement of pressure ulcer staging.

CONCLUSIONS

The results showed that the use of intermediate-frequency (10-MHz) ultrasound provides visualization of subcutaneous deep tissues and reliable identification of deep tissue injury. An unclear layered structure, hypoechoic lesion, discontinuous fascia, and heterogeneous hypoechoic area were representative findings suggesting deep tissue injury. An unclear layered structure and a hypoechoic lesion were more commonly seen in pressure ulcers with deep tissue injury than the other features, but the follow-up study suggested that discontinuous fascia and a heterogeneous hypoechoic area are more reliable predictors of future progression of pressure ulcers. It was suggested that ultrasonographic detection of deep tissue injury substantially contributes to prevention and treatment of pressure-related ulcers, although further studies involving a larger number of patients are needed to determine the value of ultrasound and to establish a standard protocol.

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