In current clinical practice, high-resolution real-time ultrasound has an established and important role in the diagnosis and management of breast disease. It is used as an adjunct to mammography and clinical breast examination [1] to evaluate lesions when findings in those examinations are indeterminate. Ultrasound imaging often allows the clinician to classify a breast mass as benign or malignant by using established descriptive parameters [2]. Sonographic features used to characterize a mass include its shape, orientation, echogenicity, heterogeneity, margin characteristics, and posterior acoustic shadowing or enhancement. These characteristics can aid in assessing the level of suspicion of a mammographically indeterminate lesion, and therefore help determine if a biopsy is indicated. Ultrasound is also an efficient tool for guidance of fine needle aspiration and core biopsy of suspicious breast lesions.

Ultrasound, like all imaging modalities, is subject to inherent artifacts. For example, ultrasound images are degraded by coherent wave interference, known as 'speckle,' which gives a granular appearance to an otherwise homogeneous region of breast parenchyma [3]. Speckle reduces image contrast and detail resolution, and diminishes the ability to differentiate normal and malignant tissues within the breast. Speckle artifact reduces the conspicuity of small, low contrast lesions and masks the presence of calcifications, an important indicator of possible malignancy. Conventional ultrasound images also exhibit a form of acoustic noise, known as 'clutter,' that arises from side-lobes, grating lobes, multi-path reverberation, and other acoustical phenomena. Clutter consists of spurious echoes, which can often be visualized within a breast cyst. Clutter may lead to concern whether a cyst is truly 'simple,' or whether it is a complex cyst that contains purulent matter or hemorrhage.

In conventional ultrasound, the breast is insonified from a single direction, and thus all the ultrasound beams are parallel, as portrayed in Figure 1a.

High resolution real time ultrasound has an established and important role in the diagnosis and management of breast disease.

Fig. 1. Comparison of conventional and compound acquisition with a linear-array transducer.

Fig. 1a. Conventional acquisition: all scan lines are parallel to each other, and perpendicular to the face of the transducer.

Fig. 1b. Compound acquisition: successive frames use different steering angles. The outermost regions of the compound image may not be included in the display.

Ultrasound, like all imaging modalities, is subject to inherent artifacts.
Compound imaging combines overlapping frames to form a real-time compound image.

This gives rise to ‘acoustic shadowing’ artifacts behind high-attenuation structures, and 'acoustic enhancement' artifacts behind low-attenuation structures. In some cases, these artifacts provide useful diagnostic criteria. Central shadowing is frequently associated with malignant solid lesions, and posterior enhancement is characteristic of simple cysts [4]. However, shadowing can also confound the diagnostic process. Strong shadows can obscure anatomy posterior to an attenuating mass. Small spurious shadows, cast by refraction from normal or benign anatomic structures, can be distracting and misleading. The sonographer must maneuver the transducer to view suspicious shadows from a variety of angles to verify the origin of the artifact, and exclude a small, occult malignancy.

Conventional ultrasound is also prone to reflection artifacts from specular (mirror-like) reflectors, such as those that arise from thin pseudocapsular margins, lactiferous ducts, and connective tissue within fat lobules. Because of the single ‘look direction’, those portions of specular structures perpendicular to the ultrasound beams produce strong echoes or ‘glints,’ but tilted or ‘off-axis’ reflectors may produce weak echoes, or no echoes at all (acoustic ‘drop out’). This, especially when combined with speckle artifact, produces a discontinuous appearance of structures which are, in fact, curvilinear and continuous.

Real Time Spatial Compound Imaging technology

The application of compounding principles to real-time ultrasound imaging is not new [4,5,6], but the practical implementation of this technology has only recently been made possible by the substantial computational power of modern, all-digital ultrasound systems. Compound Imaging starts by acquiring multiple frames from different viewing angles, as shown in Figure 1b. These overlapping frames are then combined to form a real-time compound image on the display. Compound Imaging can be implemented on a conventional ultrasound system, with two modifications.

First, the beamformer electronics must be programmed to acquire ultrasound beams that are steered ‘off-axis’ from the orthogonal beams used in conventional ultrasound. The number of frames and steering angles varies, depending on the transducer characteristics and the clinical application. In general, the more frames in the compound acquisition sequence, the better the compound image quality.

Second, the image processor must be programmed to accurately render the steered frames into the appropriate display geometry, and then combine them by frame averaging. The compound image is updated as each new frame is acquired, so there is no reduction in frame rate. However, frame averaging introduces a ‘persistence’ effect, with the potential for image blurring if the transducer or the target move too rapidly. In general, the more frames in the acquisition sequence, the greater the improvement in image quality and the greater the potential for motion blurring. This results in a tradeoff between image quality and the potential for motion blurring.
between improving image quality and minimizing motion blurring. However, this tradeoff can be optimized differently for different clinical applications. In addition, the availability of a 'survey' mode which minimizes blurring, and a 'target' mode which maximizes image quality, can be used to optimize Real Time Spatial Compound Imaging for different scanning protocols.

The ability of Compound Imaging to improve image quality primarily depends upon suppressing image artifacts. In principle, scanning from different angles produces different artifact patterns. Averaging these independent frames suppresses the artifacts and reinforces real structures. The greatest improvement occurs in the central, triangular region of the image where all the component frames overlap. Less improvement occurs in the peripheral regions of the image where fewer frames overlap.

For example, frames acquired from sufficiently different angles contain independent random speckle patterns. Frame averaging reduces the random brightness fluctuations due to speckle. The significance of speckle reduction can be appreciated in Figure 2, which shows reduced speckle and improved tissue differentiation of fat and fibroglandular tissues. The speckle signal-to-noise ratio (SNR) is an objective figure-of-merit for quantifying the amount of speckle in an ultrasound image [8]. Compound imaging can improve the speckle SNR by as much as a factor of the square root of N, where N is the number of overlapping frames. With five frames, Compound Imaging improves the speckle SNR.
Compound imaging suppresses clutter.

Central shadowing is concentrated behind the structure.

Refractive shadowing is suppressed.

Compound imaging significantly reduces speckle by more than a factor of two compared to conventional ultrasound.

Compound Imaging also suppresses the clutter obtained from different viewing angles. This is demonstrated in Figure 3, which shows significant clutter reduction in a simple cyst. The continuity of specular reflectors should also be improved by Compound Imaging, because a larger portion of each specular structure will be perpendicular to one of the different steering angles. This is depicted in Figure 4, which shows improved linearity and continuity of the branching ductal structures in the breast.

Compound Imaging is expected to preserve central acoustic shadowing and enhancement, which are important sonographic characteristics. In a compound acquisition of a lesion with central shadowing, shadows caused by attenuation within the lesion will be cast in different directions, as shown in Figure 5. When the frames are averaged, the non-overlapping portions of the shadows will be diminished, while the overlapping shadows immediately behind the lesion are reinforced. Thus, central shadowing (and likewise enhancement) should not be eliminated, but concentrated in an elongated triangular region behind the structure that causes it. The enhancement posterior to a fibroadenoma, represented in Figure 6, demonstrates this effect.

Another source of shadowing is refraction of the ultrasound beam by normal or benign anatomic structures, such as blood vessels, cysts, pseudo-capsules around solid nodules, or Cooper's ligaments. Refractive shadows hinder the diagnostic process because they can mimic the central shadows from small occult malignancies. However, the etiology of refractive shadowing is entirely different. Refractive shadows only occur when the ultrasound beam encounters a tissue interface at certain 'critical' angles. Compound Imaging acquires frames from multiple angles, so a refractive shadow is not likely to be present in each frame. Therefore, frame averaging suppresses the refractive shadow. By contrast, central shadows from malignancies arise from acoustic attenuation of the beam, which is independent of incident beam angle. Figure 6 demonstrates that Compound Imaging suppresses the refractive edge shadows from the pseudo-capsule of a fibroadenoma. In order to identify refractive shadowing from Cooper's ligaments with conventional real time ultrasound, clinicians routinely scan from different angles, apply pressure with the transducer, or alter patient position. If the shadow persists regardless of scanning angle, a malignancy may be present. If the shadow disappears with transducer angulation or compression, it is probably a refractive shadow associated with a Cooper's ligament. Compound Imaging should help identify the cause of shadowing quickly, without excessive manipulation of the transducer.

Early clinical experience

The preliminary clinical evaluation of Real Time Spatial Compound Imaging was conducted at First Hill Diagnostic Imaging in Seattle, Washington. The primary objective was to assess the clinical advantages and limitations of Compound Imaging compared with conventional ultrasound for targeted breast ultrasound examinations. The equipment used was an ATL HDI 5000 ultrasound system, with an L12-5 38 and an L12-5 50 high frequency linear array transducer. The system settings were optimized for imaging the breast. The prototype software in the HDI 5000 system was modified to support both conventional and compound scanning modes. Fourteen patients were examined. They were referred for advanced staging of breast cancer, for evaluation of indeterminate mammograms, for follow up of complications of breast surgery, or for monitoring for local recurrence. Informed consent was obtained from each patient after the nature and intent of the procedure had been fully explained. The patients were evaluated with both Real Time Spatial Compound Imaging on the HDI 5000 and with conventional ultrasound on either the same HDI 5000 or on an HDI 3000. Patient medical history, previous mammograms or sonograms, and in some cases MR contrast breast studies, were used in conjunction with the ultrasound examinations.

In all fourteen cases, Compound Imaging significantly reduced the appearance of speckle and improved contrast resolution. Compound images were qualitatively smoother, with no apparent loss of detail. The echo amplitude and texture of fat were strikingly differentiated from glandular tissue in the breast. Compound Imaging was also found to reduce clutter, unmasking subtle underlying diagnostic details. For example, clutter...
in the hypoechoic central cores of two carcinomas was suppressed by Compound Imaging, revealing small punctate calcifications. Also, in several cases, the apparent reduction of image noise and clutter extended the depth where valuable diagnostic information was visualized. This was particularly noticeable at depths greater than three centimeters.

Compound Imaging improved the continuity of specular reflectors, such as the thin, echogenic pseudo-capsule around a fibroadenoma. Although capsular margins were evaluated with conventional ultrasound, this required physical manipulation (rocking and heeling) of the transducer to view the margin from various angles, as described by Stavros et al. [2]. The multiple steering directions employed by Compound Imaging improved the continuity of specular reflectors in real time, without significant physical manipulation of the scanhead. Lateral boundaries of masses, where conventional ultrasound is more subject to ‘drop out,’ were particularly improved by Compound Imaging. Striations within fat lobules and pectoral muscle were markedly more apparent and continuous with Compound Imaging. Depiction of the internal architecture of solid lesions was also improved.

The effect of Compound Imaging on acoustic shadowing and enhancement was also evaluated. In all three lesions with central shadowing (2 malignant masses and 1 benign solid mass) central shadowing was preserved with Compound Imaging. Figure 7 shows that central shadowing was maintained even for a small (9 mm) malignant mass. Posterior acoustic enhancement was also preserved, or became more conspicuous, Echo amplitude and texture of fat were strikingly differentiated from glandular tissue.

**Central shadowing and posterior acoustic enhancement were preserved.**
for all eleven enhancing lesions (10 simple cysts and 1 fibroadenoma). Figure 8 demonstrates posterior acoustic enhancement even in the smallest (3 mm) of these cysts. Preservation of central shadowing and enhancement is an important finding, because it suggests that established diagnostic criteria can be used with Compound Imaging. As expected, a significant reduction in refractive shadowing and the improved definition of the spiculated lateral boundaries, characteristic of malignancy.
shadowing was noted with Compound Imaging, including those arising from the lateral edges of a pseudo-capsular fibroadenoma, and from Cooper’s ligaments, depicted in Figure 9. This reduction in refractive shadowing observed with Compound Imaging was considered beneficial because it allowed the clinician to classify shadows quickly, without excessive manipulation of the transducer. Also, structures deep to the Cooper’s ligament were better visualized with Compound Imaging, such as the fat lobule depicted in Figure 9.

Ultrasound is frequently used to survey the entire breast. Even in a targeted exam of a palpable lesion, the clinician may rapidly scan the remainder of the breast and adjacent tissues in search of multi-focal disease or nodal involvement. Since Compound Imaging involves frame averaging, there is a potential for motion blurring in rapid examinations. During this evaluation, the clinician sometimes began scanning with Compound Imaging in ‘survey’ mode, which uses few component frames to minimize motion blurring. Once an area of interest was identified, a ‘target’ mode was employed to maximize image quality by using a large number of component frames. For a palpable lesion, the ‘target’ mode was used first, followed by a survey of the remainder of the ipsilateral breast and the contralateral breast. In either case, the availability of ‘survey’ and ‘target’ modes was considered useful, with the clinician able to make an appropriate choice for the clinical situation. Table 1 summarizes the observed characteristics and clinical impacts of Real Time Spatial Compound Imaging. In most cases, the image quality improvements – while significant - did not affect the diagnosis. However, in one case Compound Imaging did change the diagnostic conclusion of the examination. The following case study illustrates the potential of Real Time Spatial Compound Imaging in a clinical diagnostic setting.

**Case study**

A 33-year-old woman with a single palpable breast mass, electing non-operative alternative medical therapy, was referred for conventional ultrasound (HDI 3000). The lesion was heterogeneous with irregular margins, and was classified as malignant by mammography and ultrasound. This mass demonstrated a hyperechoic outer margin and a hypoechoic central core, as represented in Figure 10. On further examination with Real Time Spatial Compound Imaging, several punctate calcifications were well visualized within the central core. Retrospectively, the calcifications could be identified with conventional ultrasound, but were very difficult to confidently separate from clutter artifacts. Real Time Spatial Compound Imaging

<table>
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<th>Image Characteristic</th>
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<td>Increased conspicuity of low contrast lesions</td>
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<td>Clutter reduction</td>
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<td>Better detection of calcifications</td>
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<td>Continuity of specular reflectors</td>
<td>Enhanced delineation of capsular margins, ducts, and connective tissue</td>
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<td></td>
<td>Improved depiction of internal architecture of solid lesions</td>
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<tr>
<td>Preservation of central acoustic shadowing</td>
<td>Maintain established diagnostic criteria for cysts and solid lesions</td>
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<td>and acoustic enhancement</td>
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<td>Reduced refractive shadowing</td>
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<td>Improved visibility of structures posterior to Cooper’s ligaments</td>
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<td>Persistence due to frame averaging</td>
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<td>Mitigated by ‘Target’ and ‘Survey’ modes optimized for intended use</td>
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Table 1. Summary of observations for Real Time Spatial Compound Imaging

Several punctate calcifications were revealed.

A small satellite lesion was also revealed.
Compound imaging enhances image quality by reducing artifacts.

Real Time Spatial Compound Imaging can positively impact the diagnosis and management of breast lesions.

Fig. 10. Infiltrating ductal carcinoma.

Fig. 10a. Conventional image: a 2 cm, surgically proven carcinoma. It was characterized as malignant by its irregular, poorly defined and thickened margins, heterogeneity, hypoechoic core, and vertical orientation.

Fig. 10b. Compound image: small punctate calcifications, an additional characteristic of malignancy, are revealed within the central core of the lesion. They could only be identified retrospectively with conventional real-time ultrasound.

Fig. 11. Satellite lesion.

Fig. 11a. Conventional image: a 3 mm carcinoma (arrow), situated 1 cm medial to the primary lesion, was missed prospectively on physical breast examination, mammography, and conventional ultrasound.

Fig. 11b. Compound image improvements in speckle and clutter reduction allowed this small malignant lesion to be detected with Compound Imaging. Once found, the satellite lesion could be identified retrospectively on the mammogram and with real-time conventional ultrasound. Detailed pathological examination of the breast specimen confirmed a satellite lesion of this size in this location.

Also revealed a small (3 mm) previously missed satellite lesion adjacent to the primary tumor, as shown in Figure 11. The Compound Image of the satellite lesion showed the same echogenic rim and hypoechoic central core as the primary tumor. The satellite lesion was then evaluated retrospectively with conventional ultrasound. Although it could be seen in hindsight, the lesion’s appearance was so subtle that three experienced clinical observers agreed that without Compound Imaging, this structure would not have been identified prospectively. The satellite lesion was then retrospectively located on one of the mammograms.

Based in part on these multi-focal findings, the patient opted for more aggressive treatment. Upon subsequent surgery, both the primary and satellite malignancies were confirmed by pathology.

Conclusion

Real Time Spatial Compound Imaging is now a practical reality, due to the computational power of modern, all-digital ultrasound systems. Compound imaging enhances image quality by reducing image artifacts inherent to conventional ultrasound. In the future, comparative studies with larger numbers of cases will be needed for a more complete assessment. However, this early clinical experience shows that Real Time Spatial Compound Imaging has the potential to positively impact the diagnosis and management of benign and malignant disorders of the breast.
References


