VALUE OF REAL-TIME COMPOUND SONOGRAPHY IN FINE NEEDLE ASPIRATION BIOPSY OF THYROID NODULES: A COMPARATIVE STUDY

TİROİD NODÜLLERİNİN İNCE İĞNE ASPİRASYON BİYOPSİSİNDE GERÇEK-ZAMANLI 'COMPOUND' GÖRÜNÜTÜLEMENİN DEĞERİ: KARŞILAŞTIRMALI ÇALIŞMA

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ABSTRACT

Purpose: *Real-time compound imaging is one of the main advances in sonographic technology. Our aim was to assess the potential benefits of real-time compound sonography in the fine needle aspiration biopsy of the thyroid nodules compared with conventional sonography.* ***Methods:*** *Sonography-guided fine needle aspiration biopsy was performed on 60 thyroid nodules of 60 consecutive patients. Sonograms of the same nodule were obtained during the biopsy procedure using both conventional sonography and compound imaging. All images were independently reviewed by two independent observers experienced in sonography. For all images, the visibility of the needle shaft, visibility of the needle tip, and overall image quality were assessed and graded. Wilcoxon's signed rank test was used for statistical comparisons between the two techniques. Kappa scores were calculated to assess inter-observer agreement.* ***Results:*** *Real-time compound imaging was significantly superior to conventional sonography with respect to overall image quality, and visibility of the needle shaft and the tip, compared to conventional sonography ($p<0.001$ for all evaluated parameters). In none of the images was the visibility of needle tip better in conventional images according to both observers.* ***Conclusion:*** *In terms of overall image quality, and the visibility of the shaft and tip of the needle, real-time compound sonography is superior to fundamental sonography in guiding the biopsy needle ultrasonographically. We assume that real-time compound imaging can be used for guidance in fine needle aspiration biopsy, and may be especially helpful for less experienced radiologists by way of easier visualization of the needle and its relationships with the lesion and neighboring structures.*

Key Words: *Thyroid Nodules Compound İmaging Fine Needle Aspiration Biopsy.*

ÖZET

Amaç: *Gerçek zamanlı "compound" görüntüleme ultrasonografi teknolojisinde önemli ilerlemelerden biridir. Çalışmamızda gerçek zamanlı "compound" ultrasonografinin konvansiyonel ultrasonografi ile karşılaştırıldığında, tiroid nodüllerinin ince iğne aspirasyon biyopsisindeki potansiyel faydalarını değerlendirmeyi amaçladık.* ***Method:*** *Bu çalışmada, 60 ardışık hastada 60 tiroid nodülüne ultrasonografi kılavuzluğunda ince iğne aspirasyon biyopsisi uygulandı. Biyopsi işlemi sırasında aynı nodülün hem konvansiyonel hem de "compound" görüntüleme ile ultrasonogramları elde edildi. Tüm görüntüler ultrasonografide deneyimli birbirinden bağımsız iki gözlemci tarafından değerlendirildi. Tüm görüntüler için, iğne şaftının görünebilirliği, iğne ucunun görünebilirliği ve genel görüntü kalitesi değerlendirildi ve derecelendirildi. İki teknik arasında istatistiksel kıyaslama için Wilcoxon işaret testi kullanıldı. Gözlemciler arasındaki uyumu değerlendirmek için Kappa skorları hesaplandı.* ***Bulgular:*** *Gerçek zamanlı 'compound' görüntüleme, iğne şaftının ve ucunun görülebilirliği, ve genel görüntü kalitesi bakımından konvansiyonel US'ye göre daha üstündü (tüm değerlendirme kriterleri açısından $p<0,01$). Her iki gözlemci için de görüntülerin hiçbirinde iğne ucunun görülebilirliği açısından konvansiyonel US, gerçek zamanlı 'compound' görüntülemeye göre daha iyi değildi.* ***Sonuç:*** *Genel görüntü kalitesi, iğne şaftının ve ucunun görülebilirliği göz önüne alındığında gerçek zamanlı 'compound' görüntüleme, biyopsi iğnesine ultrasonografik kılavuzluk etmede konvansiyonel sonografiye üstündür. İğnenin ve iğne ile lezyon ve komşu yapıların ilişkisinin daha kolay görülebilir hale gelmesi nedeniyle, gerçek zamanlı 'compound' görüntüleme, özellikle az deneyimli radyologlara biyopsi işlemi sırasında yardımcı olabilir.*

Anahtar Kelimeler: *Tiroid Nodülü Compound Gözeneklerine İnce İğne Aspirasyon Biyopsi.*

INTRODUCTION

In current clinical practice, sonography plays an important role in the diagnosis and management of thyroid nodules. One of the most useful roles of sonography is accurate guidance of fine needle aspiration biopsy (FNAB), which is well established as a safe, simple and cost effective diagnostic tool in the evaluation of thyroid nodules (1-7).

In many cases, however, conventional sonography displays a number of inherent artifacts that compromise image quality and limit diagnostic ability. Real-time compound imaging (RTCI) is one of the main advances in sonographic technology. Compound sonography acquires information from several different angles of insonation and merges them to produce a single compound real-time sonographic image. In that way compound imaging overcomes the inherent artifacts of conventional sonography that degrade image quality (8-12). Early clinical and in vitro studies have demonstrated that this method improves contrast resolution and tissue differentiation of superficial soft tissue structures as well as of abdominal and pelvic lesions. It is also stated that compound imaging leads to more detailed visualization of specularly reflecting interfaces, such as biopsy needles (13-16). The purpose of our study was to assess the potential benefits of real-time compound sonography in the FNAB compared with conventional imaging.

MATERIALS AND METHODS

From January to May 2004, sonography-guided FNAB was performed on the thyroid nodules of 60 consecutive patients referred to our institution. The mean age of the patients was 45.05 ± 13.6 years, with ages ranging from 18 to 73 years. Forty-one patients were female and 19 were male. The size of the nodules ranged from 7 to 30 mm (mean size 16.03 ± 5.6).

Sonographic examinations of all patients were performed with an HDI 5000 system (Philips-ATL, Bothell, WA, USA) using a 5-12 MHz multifrequency linear array transducer. All biopsies were performed by the same experienced radiologist using a 20-gauge aspiration needle with the freehand technique. The patient was placed in the supine position with slight hyperextension of the neck. The skin overlying the neck was cleaned with a povidone-iodine 10% solution after the initial sonographic evaluation of the thyroid nodule. Local anesthetic was not routinely applied. The sonography probe was covered with a sterile cover and placed on the neck perpendicular to the thyroid gland. The nodule was localized in the transverse plane and the transducer was adjusted to center the nodule in the sonographic image. The needle was inserted parallel to the ultrasonographic plane next to the medial edge of the transducer so that the entire length of the needle could be seen as it entered the thyroid nodule. Once the shaft and the tip of the needle were localized within the appropriate area of the nodule for biopsy, sonographic images were obtained using conventional sonography first, followed by RTCI. The plane of imaging was kept as constant as possible while switching between conventional sonography and RTCI. Imaging parameters and instrument settings were not changed between different modes. Specimens were obtained with gentle suction applied by withdrawing 2-3 ml in the plunger of a 10 ml syringe. The needle was withdrawn after the suction was released. The material was then smeared onto glass slides that were fixed in 95% ethyl alcohol afterwards. No complication occurred in any of the patients.

For a partially cystic nodule the biopsy sampling was directed to the solid portion of the nodule to optimize the cellularity of the specimen. In patients with more than one nodule FNAB was performed on the largest one only.

'Target' and 'survey' modes of compound imaging were available in our ultrasound system. The survey mode produces three coplanar images during the compound acquisition that minimize blurring and allow rapid scanning. The target mode, on the other hand, produces nine coplanar images that maximize the image quality, with an increased potential for motion blurring. In our study we used the survey mode in order to reduce blurring and to preserve the frame rate.

A set of two sonograms of the same nodule was obtained during the biopsy procedure using conventional sonography and RTCI. The image sets obtained for each procedure were randomly mixed and displayed on a computer monitor side by side. Digitally stored images were independently reviewed and rated by two observers experienced in US. For all images, the visibility of the needle shaft, visibility of the needle tip, and overall image quality were assessed and graded. The readers were blinded to the respective mode by covering the system parameter displays on stored images. Observers independently graded the images using a three-point scale for the defined parameters as follows: 0 poor, 1 moderate, and 2 excellent image quality. Overall image quality was articulated as a general assessment encompassing spatial resolution or detail, solid-cystic differentiation, and absence of noise and artifacts such as speckle, reverberation, clutter, or blurring. Additionally, the visibility and clarity of the appearance of the needle shaft and tip were evaluated. All patients provided informed consent and institutional review board approval was obtained.

Statistical analysis was performed with a commercially available statistical software program (SPSS 11.0, Chicago, IL, USA). Wilcoxon's signed rank test was used for statistical comparisons between the conventional sonography and RTCI. Kappa scores were calculated to assess inter-observer agreement and a p value of less than 0.05 was considered significant.

RESULTS

Kappa scores ranged from 0.396 to 0.834 ($p<0.05$), reflecting a moderate to substantial inter-observer agreement.

Mean scores of each technique for the evaluated parameters are summarized in Table 1. Regarding the overall image quality, conventional images received a mean score (±SD) of 0.85 ± 0.48, whereas the mean score for compound images was 1.52 ± 0.50. For visibility of the needle shaft, conventional and compound images received mean scores of 0.86 ± 0.54 and 1.69 ± 0.53, respectively. Mean scores for visibility of the needle tip in conventional and compound images were 0.83 ± 0.59 and 1.66 ± 0.47, respectively. In none of the images was the visibility of needle tip better in conventional images for both observers. Statistical analysis revealed that RTCI gave significantly improved overall image quality, and visibility of the needle shaft and tip, compared to conventional sonography ($p<0.001$ for all evaluated parameters).

Table-1: Mean scores of conventional sonography and real-time compound sonography *.

Conventional	Sonography	RTCS
Overall Image Quality	0.85 ± 0.48	1.52 ± 0.50
Visibility of Needle Shaft	0.86 ± 0.54	1.69 ± 0.53
Visibility of Needle Tip	0.83 ± 0.59	1.66 ± 0.47

Note.- Three-point scale for the defined parameters: 0 poor, 1 moderate, and 2 excellent image quality. RTCS = Real-time compound sonography.

Of these 60 patients, adequate cells were present for cytologic analysis in 51 nodules, yielding a diagnostic rate of 85%. In the remaining 9 nodules (15%) the aspirate was inadequate for diagnosis. Among the patients in whom FNAB was considered diagnostic, the cytologic findings were non-neoplastic (including colloid mixed with follicular cells) in 29/60 (48.33%), inconclusive (follicular or Hurthle cell neoplasia) in 17/60 (29.33%), suspicious for malignancy in 3/60 (5%), and malignant (papillary carcinoma) in 2/60 (3.33%).

DISCUSSION

Thyroid nodules are commonly seen and most of them are benign. The incidence of sonographically visible nodules in the general population is approximately 10-40% (17,18). These lesions may present as a clinically palpable nodule or as an entirely incidental finding detected during imaging examinations performed for other indications. Sonography is an extremely useful diagnostic tool for detecting nodules and evaluating features that increase the likelihood of malignancy (19,20). However, there is considerable overlap of characteristic findings in benign and malignant nodules, as documented by many studies. Some authors have even suggested that sonography should only be used to determine the presence of focal lesions, to find out if a lesion is cystic or solid, and for guiding the needle for biopsy (19-23). FNAB, which is a minimally invasive yet safe procedure, is currently considered the most reliable diagnostic tool for the evaluation of thyroid nodules (24-26). The procedure is useful for separating patients requiring surgery from those requiring suppressive or other forms of medical therapy. It has been reported that sonographically guided FNAB provides a higher rate of diagnostic accuracy than does FNAB without US guidance, even in clinically palpable nodules, because the needle can be visualized continuously during insertion and needle sampling from various portions of the nodule is possible. Sonographic guidance is especially useful in sampling small nodules, which are not always easily palpable, and nodules located in firm, lobulated thyroid glands (6,27,28).

Acquiring sufficient aspirate is critical for making a correct diagnosis. However, different cytohistological studies revealed that the rates of achieving adequate specimen cellularity varied from 68% to 96.6% (3,29,30). This inconsistency can be attributed to a number of factors including operator skill, large body habitus of the patients, and difficult lesions, such as small or deeply located nodules. The relatively high incidence of inconclusive results and insufficient aspirate are the main drawbacks of FNAB. In our study this occurred in 9 of 60 patients (15%), a rate similar to those of other series. Inadequate specimens seem to be caused mostly by aspiration of blood, cystic fluid or both, with a paucity of follicular epithelial cells from the lesion (25). Higher rates of obtaining sufficient aspirates can be achieved with less influence from the mentioned factors. We tested the hypothesis that using compound imaging may be helpful for better visualization of the nodule and the needle, consequently improving the success of the biopsy procedure, in obtaining material from an appropriate location, such as the solid portion of a cystic lesion.

Like all other imaging modalities, conventional sonography is still subject to inherent artifacts compromising the image. RTCI is one of the innovative technologies introduced in recent years to improve ultrasound image quality. Although the principles and benefits of compound imaging have been known since the 1950s, it has been available only recently with the extensive computational power of modern all-digital US systems. Real-time compound imaging uses computed beam steering technology to acquire multiple coplanar tomographic images from different viewing angles and combines and averages these to form a single compound real-time image. Scanning from different viewing angles produces different artifact patterns, substantially reducing the artifacts such as clutter, speckle, glint, dropout and refractive shadows (8-11,13-15). In compound imaging, increased blurring and a slow frame rate are expected to occur, even though shadowing artifacts are reduced. The blurring is due to the longer time required for averaging the frames obtained from multiple pulses and displaying the summated image, and it may limit the detectability of subtle details. In RTCI, however, the frame numbers and steering angles can be used, depending on the type of transducer and the clinical application, and in this way blurring can be controlled to a certain degree. The more frames in the compound acquisition sequence, the better is the image quality of the compound sonography (31). In our study we decided to use the 'survey' mode of our US system, which produces three coplanar images during the compound acquisition, reducing blurring, and simultaneously allowing rapid scanning, which preserves the frame rate.

Signals from specular reflectors are reduced or lost in conventional imaging when their interfaces do not lie at 90 degrees to the insonating sound beam. In addition, speckle and clutter add noise and reduce image contrast. It is suggested that compound imaging improves the delineation of specularly reflecting interfaces with much fewer artifacts degrading the image, reduces speckle size by speckle averaging, and improves spatial resolution, leading to a more complete visualization of specular reflectors (32). By generating an image from multiple scan lines, real-time CI enhances image contrast, allowing superior definition of specular reflectors like the margins of organs and lesions, as well as biopsy needles. RTCI reduces the grainy appearance in sonograms by suppressing the speckle and improves the signal-to-noise ratio, which should also improve the visibility of the needles (13,15,33).

Compound imaging is reported to be useful in the demonstration of thyroid nodules, providing better nodule conspicuity and greater freedom from artifacts (33). Decreased artifactual echoes within the lesion may improve the solid-cystic differentiation as well. Reduced noise and speckle in compound imaging eliminates artifacts in liquid cavities, making the true echoes from the solid portion more conspicuous. In our study we did not compare the results of biopsies from cystic lesions separately, since the number of cystic lesions was small. However, our observation is that it is an excellent method for precisely positioning the needle in the solid portion of complex nodules and avoiding a puncture across dense calcifications, which would potentially increase the diagnostic accuracy of the procedure.

Real-time compound sonography has been reported to improve contrast resolution, tissue differentiation and overall image quality in breast, vascular and musculoskeletal imaging, primarily by reducing unwanted artifacts without compromising other beneficial image characteristics like spatial resolution (13-15). In our study we investigated the usefulness of RTCI in the FNAB of thyroid nodules. According to Saleh et al., real-time compound sonography improves the visibility of needles and localization of wires compared to single-line ultrasonography. Particularly for steeper angulations of the needle the image contrast was enhanced with RTCI, and it was suggested that it may be useful for increasing the precision of ultrasound-guided percutaneous interventions (34). In accordance with this study, our own results showed that RTCI significantly improves the visibility of the shaft and tip of the needle. Although the needles were also perceivable with conventional US in most cases, this required physical manipulation of the transducer to view the exact location of the needle. The multiple steering directions employed by compound imaging create

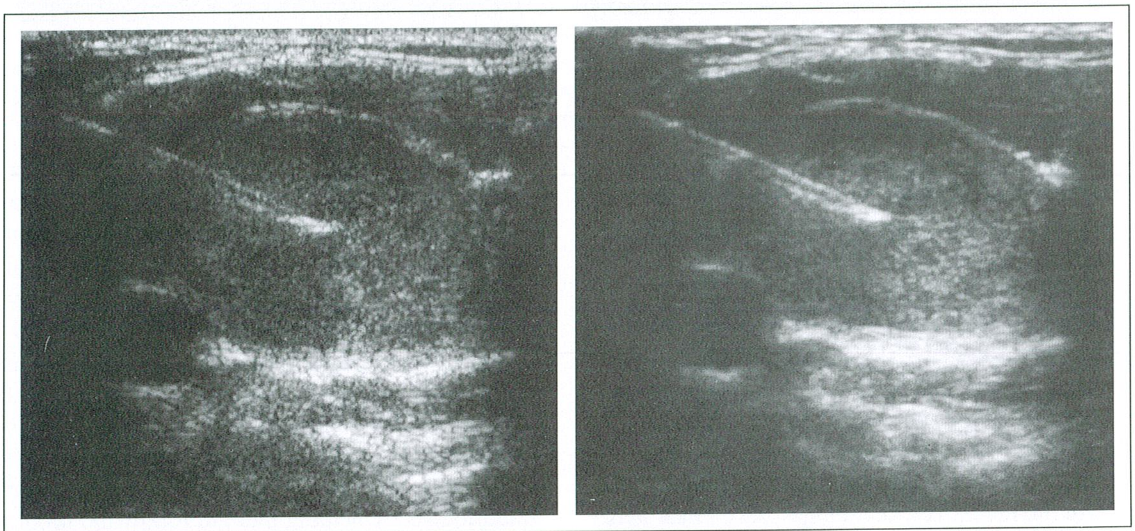

Fig. 1: A 27-year-old woman with a nodule located in the right lobe of the thyroid gland. The conventional sonographic image during the biopsy procedure shows the location of the needle shaft and the tip (a). Compound sonography shows less artifact and better visualization of the needle shaft and the tip compared to conventional imaging (b).

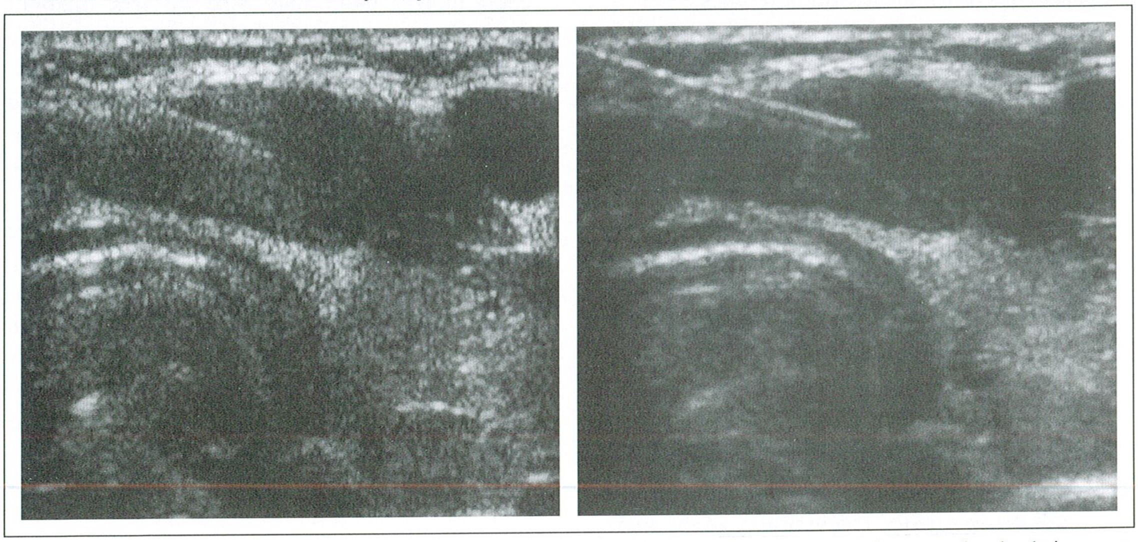

Fig. 2: An isthmic nodule in a 37-year-old male. Compared to conventional sonography (a), compound sonography clearly improves the visualization of the needle shaft and tip (b).

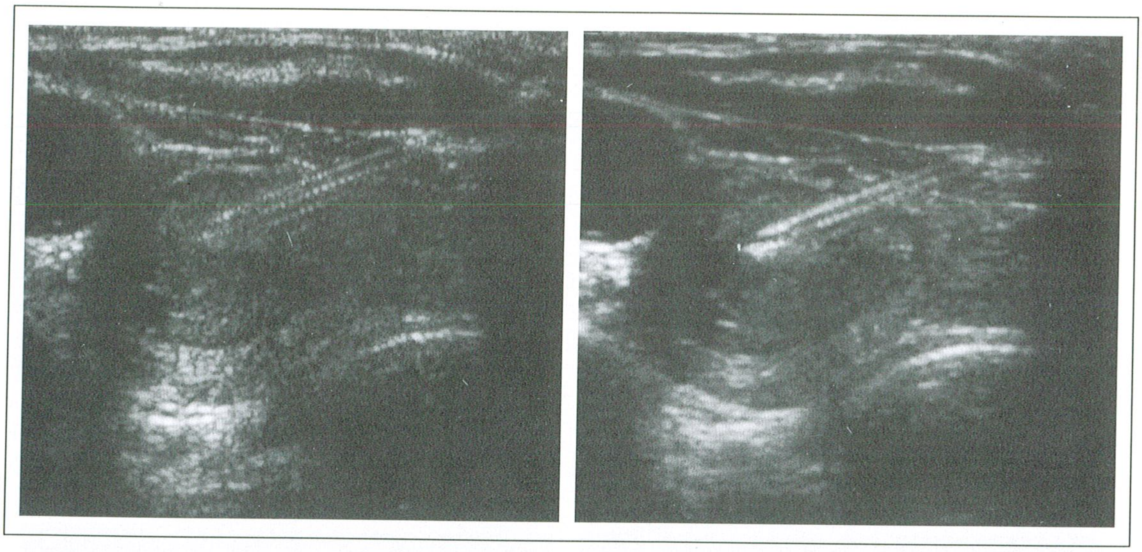

Fig. 3: Conventional (a) and compound sonographic images (b) of a right-sided thyroid nodule, in a 51-year-old woman, obtained during the biopsy procedure. Compound sonography shows the needle shaft, even the inner stylet, much better than the conventional sonogram. Also note the much brighter needle tip than in the conventional sonogram.

significantly more reflectance from the needle, turning it into a brighter object within the tissue. Consequently the visibility of the whole shaft and the tip of the needle was improved (Fig. 1, 2). Depiction of the internal architecture of the solid nodule was also improved and the artifacts and noise were reduced, improving overall image quality. Since RTCI uses multiple scanning angles to generate each image there may furthermore be less operator dependence on achieving optimal scanning angles. We think that, due to the mentioned advantages, RTCI may help less experienced radiologists to visualize the needle better and more easily, and to perform biopsies with more successful outcomes.

The posterior echo pattern is less in RTCI, which is actually helpful in localizing the needle tip during the biopsy procedure. Yet, the tip is more visible in RTCI since it shows echo-strong structures better than conventional imaging (Fig. 3).

The limitation of this study was that the images displayed on the computer for the evaluation of observers had no parameters on them for the purpose of blinding. However, that was difficult to achieve because of the considerable differences in image quality between conventional and compound images.

The results of our study showed that, in terms of overall image quality, and visibility of the shaft and tip of the needle, RTCI is superior to fundamental sonography in guiding the biopsy needle ultrasonographically. These findings show close correspondence with the theoretical advantages of RTCI. Even though the FNAB of the thyroid has been regarded as the most effective method for diagnosing the malignancy, the diagnostic accuracy of FNA cytology is far from ideal, partly due to improper localization of the needle. The accuracy of the FNAB procedure depends on operator skill and experience. RTCI may also be useful for less experienced radiologists by helping them to follow the needle tract and observing the tip of the needle. Because RTCI uses multiple scanning angles to generate each image, there may also be less operator dependence on achieving optimal scanning angles. We assume that RTCI can be used for guidance in fine needle aspiration biopsy, and may be especially useful for the depiction of lesion boundaries that are difficult to visualize with fundamental imaging, and in avoiding the cystic parts of the lesion during the biopsy. The question of whether compound imaging can decrease the amount of false negative results needs to be addressed in further studies with larger series. Furthermore, additional research is required to determine whether similar improvements are observed in other anatomic areas.

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