Ultrasound elastography (USE) describes a variety of ultrasound-based imaging techniques that measure tissue stiffness properties, and is currently under intense investigation for tissue characterization in several anatomic sites. This article summarizes the evidence regarding the accuracy of USE for malignancy in the head and neck. Currently, most published data pertains to small pilot studies with varied methodologies. Encouragingly, most studies have documented promising results for USE in terms of high accuracy for malignancy in thyroid nodules and cervical lymph nodes, which have surpassed conventional sonographic criteria. However, a minority of studies have documented opposite findings. USE seems to be suboptimal for salivary malignancies, and some evidence suggests that USE does not provide useful diagnostic information compared with conventional ultrasonography for miscellaneous neck masses. Further larger studies are required to validate these findings although, in view of the predominance of highly optimistic results for thyroid nodules and cervical lymph nodes, USE may become a useful ancillary technique in the routine diagnostic work-up of lesions in these tissues in the near future.

Keywords: Ultrasound; elastography; acoustic radiation force impulse; shear wave elastography; thyroid; lymph nodes; salivary glands; neck.

Introduction

High-resolution ultrasonography (US) is a sensitive imaging test for the detection of thyroid nodules, cervical lymph nodes, salivary masses and other superficial neck masses. In experienced hands, many neck lesions can be diagnosed using a combination of grayscale and power Doppler sonographic features. Nevertheless, it is widely recognized that conventional US has limited accuracy for malignancy in these sites. In recent years, multiple pilot studies have evaluated ultrasound elastography (USE) for cancer detection in the head and neck. In a previous article, the basic principles and practical issues of USE were outlined. This article summarizes the published evidence for the accuracy of USE in these sites.

USE for evaluation of thyroid nodules

Thyroid nodules present a considerable diagnostic challenge. Several sonographic criteria have predictive value for malignancy (e.g. irregular margins, punctate microcalcifications, hypoechogenicity, taller than wide shape, etc.) although no single criterion or combination of criteria achieves a balanced high sensitivity and specificity[1–7]. US-guided fine-needle aspiration cytology (FNAC) has a high specificity for malignancy (60–98%). Nevertheless, FNAC cannot be performed for all thyroid nodules because they are extremely common (~50%) and only a small proportion (~<5%) are malignant[8,9]. Furthermore, even for nodules undergoing US-guided FNAC, the sensitivity for malignancy may be suboptimal.
(54–90%) because the specimens may be inadequate, non-representative, or indeterminate in the case of follicular lesions.\textsuperscript{[10–15]}

At the time of writing, around 40 pilot studies have been published evaluating thyroid USE for malignancy, with sample sizes ranging between 16 and 912 nodules.\textsuperscript{[16–55]} Study methodologies have varied widely in terms of nodule selection criteria, thyroid biochemical status, USE technology, acquisition technique, elastographic scoring system, and use of FNAC or surgical pathology as reference standards. For valid ethical reasons, most pilot studies have comprised only those nodules scheduled for FNAC or surgery as per routine diagnostic work-up. This approach has restricted samples to nodules that are suspicious or indeterminate for malignancy on conventional US criteria or previous FNAC, or

\textit{Figure 1} Longitudinal grayscale US image with corresponding strain elastogram of an irregular hypoechoic thyroid nodule containing multiple foci of punctate calcification (arrow). This nodule appears red on the elastogram, suggestive of a stiff nodule. FNAC confirmed papillary thyroid carcinoma.

\textit{Figure 2} Longitudinal grayscale US image with corresponding strain elastogram showing a slightly irregular hypoechoic thyroid nodule (arrow). This appears green and mauve, suggestive of a soft nodule. FNAC and imaging follow-up confirmed a benign haemorrhagic cyst.
Figure 3  Longitudinal grayscale US image with corresponding strain elastogram showing a slightly irregular hypoechoic thyroid nodule (arrow). The colour scale differs from that used in Figs. 1 and 2. The nodule appears blue, suggestive of a stiff nodule. FNAC indicated a papillary carcinoma. On this system, compression quality feedback is provided in real time in the form of a visual scale (white arrowhead) and displacement versus time graphical plot (short arrow).

Figure 4  Transverse grayscale US image with corresponding strain elastogram showing an irregular hypoechoic thyroid nodule (arrow). This appears predominantly green, suggestive of a soft nodule. FNAC confirmed a papillary thyroid carcinoma. This may be regarded as a false-negative on strain imaging.
less commonly are within a compressive goitre scheduled for surgery. In addition, thyroid strain elastography studies have excluded large or coalescent thyroid nodules, and in some cases nodules within a background thyroiditis, because of the lack of sufficient normal thyroid parenchyma in the elastogram for reference. Many real-time strain elastography (RTE) studies have also excluded nodules containing coarse calcifications or large cystic foci because evidence indicates that these factors can genuinely or artefactually increase nodule stiffness and thus may reduce the accuracy of RTE for malignancy. It is worth highlighting that all RTE studies have used freehand compression to generate elastograms although there are several reports of off-line thyroid USE using intrinsic compressions from the carotid artery as the only compressive source.

Encouragingly, most USE reports document higher stiffness indices for thyroid cancers compared with benign nodules. These findings are also supported by very limited biomechanical stiffness data from thyroidectomy specimens. In this respect, if nodules are subjected to identical test loads, the elastic modulus of malignant nodules (mean ± SD 99.7 ± 79.8 kPa) is significantly higher than that of benign nodules (22.5 ± 9.6 kPa) and normal thyroid parenchyma (12.3 ± 4.8 kPa).

For strain RTE, most studies indicate that elastographic colour patterns corresponding to minimal or no strain (typically elastographic scores (ES) ≥3) or high strain ratios (SRs) are predictive of malignancy (Figs. 1–3) although false-negatives (Fig. 4) and false-positives (Fig. 5) are documented using optimized cut-offs. A meta-analysis of 8 RTE studies performed between 2005 and 2009 (639 thyroid nodules, 24% malignancies) calculated a pooled sensitivity and specificity of 92% and 90%, respectively. Many reports suggest that RTE is an independent predictor for malignancy, with accuracy results exceeding conventional US criteria. For example, Cantisani et al. documented much higher SRs in malignant compared with benign nodules (7.3 ± 4.3 vs. 1.2 ± 0.7), and an SR cut-off ≥2 achieved 97.3% sensitivity, 91.7% specificity, 87.8% positive predictive value (PPV), 98.2% negative predictive value (NPV) and 93.8% accuracy. By comparison, sonographic criteria achieved accuracies between 38% and 81%. In the largest RTE study to date, comprising 912 nodules undergoing FNAC, RTE was an independent predictor of malignancy, achieving 77.0% sensitivity, 85.2% specificity, 36.1% PPV and 97.2% NPV. Several investigators have also performed subgroup analysis of USE results according to nodule size, and their findings suggests that RTE is accurate for nodules between 5 mm and 1 cm in maximum diameter, which includes papillary microcarcinomas. A couple of studies have documented that RTE is accurate for nodules that are non-diagnostic or indeterminate on FNAC, which may be useful to stratify nodules for subsequent surgery or conservative management. However, this is not conclusive as another study has documented opposite findings.

Figure 5 Longitudinal grayscale US image with corresponding strain elastogram showing a hypoechoic thyroid nodule (arrow). This appears predominantly red, suggestive of a stiff nodule. Surgery revealed a benign hyperplastic nodule. This may be regarded as a false-positive on strain imaging.
Despite these generally promising results, a small but significant number of reports document considerably worse accuracy results for RTE\cite{20,32,33,39,50}. In the second largest thyroid USE study to date, comprising 703 nodules, qualitative RTE achieved only 65% sensitivity, 58% specificity and 61% accuracy in comparison with 92% sensitivity, 67% specificity and 74% accuracy for conventional US. In this study, the combination of RTE and conventional US was not superior to conventional US alone\cite{39}. These suboptimal findings are not restricted to qualitative RTE. Unluturk et al.\cite{50} evaluated 237 nodules using qualitative and semi-quantitative RTE and also documented suboptimal results; the optimum cut-offs for qualitative RTE achieved 72% accuracy, 47% sensitivity and 80% specificity; SR achieved 69% sensitivity and 67% specificity (accuracy was not provided); whereas margin irregularity on grayscale US achieved 81% accuracy, 69% sensitivity and 85% specificity. There are limited data regarding the accuracy of area ratios for thyroid malignancy although this criterion appears suboptimal as an independent predictor\cite{35,38}. For example, one study documented that an area ratio $>1$ achieved 92% specificity but only 46% sensitivity\cite{35}.

To date, there are only a handful of reports that have evaluated thyroid nodules using shear wave elastography (SWE)\cite{21,29,45,51,54,60} (Fig. 6). In general, these document higher shear wave velocities or elastic moduli in malignant thyroid nodules (Figs. 7, 8). However, similar to RTE, the reported discriminatory performances of SWE have varied. For acoustic radiation force impulse (ARFI) imaging, Gu et al.\cite{29} reported a mean shear wave velocity of $3.94 \pm 1.39$ m/s in malignant nodules compared with $2.00 \pm 0.48$ m/s in benign nodules ($P<0.001$). A cut-off $>2.56$ m/s achieved a high

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**Figure 6** Transverse ARFI US images of normal parenchyma in the left thyroid lobe (top) and of a nodule in the right thyroid lobe (bottom arrow), which was a follicular neoplasm on needle cytology. The shear wave velocity in the nodule is higher than the normal parenchyma (2.43 m/s versus 1.33 m/s). Images provided courtesy of Dr Chander Lulia, Ria Clinic, Mumbai.
sensitivity, specificity and accuracy of 86.4%, 93.4% and
91.8% respectively, in comparison with 68.2%, 86.8% and
82.7% respectively for conventional US. ARFI results
from a study by Zhang et al. [54] were less discriminatory;
a shear wave velocity of 4.82 ± 2.53 m/s (mean ± sd) in
malignant nodules compared with 2.34 ± 1.17 m/s in
benign nodules, and a cut-off of 2.87 m/s achieved
75.0% sensitivity, 82.2% specificity, and 80.3% accuracy.

Three preliminary studies have evaluated thyroid
nodules using supersonic shear wave imaging (SSI). Two separate studies by Sebag et al. [45] and Veyrieres
et al. [51] documented comparable optimistic results,
whereas another study by Bhatia et al. [60] documented
less rewarding results. In this respect, Sebag et al. [45]
and Veyrieres et al. [51] documented a stiffness of
150 ± 95 kPa (mean ± sd) and 115 ± 60.4 kPa for malign-
ant nodules, respectively, and 36 ± 30 kPa and
41 ± 25.8 kPa for benign nodules, respectively. Both of
these groups reported similar optimum cut-offs (65 kPa
and 66 kPa), which achieved 85.2% sensitivity, 93.9% specificity for Sebag et al. [45] and 80% sensitivity,
90.5% specificity for Veyrieres et al. [51]. However,
Bhatia et al. [60] documented a median stiffness of
43.1 kPa, (range 12.2–187.5 kPa) for malignant nodules
and 26.2 kPa (range 7.4–132.0 kPa) for benign nodules.
Furthermore, the optimum cut-off was much lower
(42.1 kPa), and achieved 52.9% sensitivity and 77.8%
specificity. The explanation for this difference is unclear
although one postulation is that investigators in the two
studies with optimistic results had applied greater pre-
compression on the thyroid during SWE acquisitions
than Bhatia et al. [60]. This postulation is supported by
biomechanical data from resected thyroid lesions,
which documents that applying progressively higher pre-
compressions to thyroid nodules increases their mea-
sured stiffness and, importantly, the rate of increase in
stiffness is greater for malignant nodules than benign
nodules [58]. The influence of precompression on USE
results in the head and neck requires further investigation
although it has recently been shown to have influence on
strain elastography and SWE results obtained in the
breast [61].

Figure 7 Longitudinal grayscale US image with corresponding shear wave elastogram of a hypochoic thyroid nodule (arrow). The nodule appears blue with a low mean and maximum SWE stiffness of 21.6 kPa and 29.3 kPa, suggestive of a soft nodule. Histology revealed a benign hyperplastic nodule.
There are several limitations of the current evidence. Due to selection bias, most studies comprise a much higher proportion of malignant nodules (∼25%, range 5–63%) than is present in the general population (∼5%)\(^1\)\(^6\)\(^2\)\(^4\)\(^5\)\(^6\)\(^7\)\(^8\)\(^9\)\(^10\)\(^11\)\(^12\). Consequently, the accuracy results obtained from these studies, in particular the NPV and PPV, are not applicable to an unselected population. Reported accuracy results for thyroid USE are probably applicable to solid papillary thyroid cancers only, because these comprise most of the malignancies in published series (∼90%), which reflects their predominance in routine clinical practice. Moreover, there are sparse data regarding the accuracy of USE for intracystic papillary thyroid carcinoma and, importantly, for other malignancies such as follicular, medullary cell and anaplastic carcinomas. It would be prudent to address these deficiencies, especially because follicular lesions are relatively common and cannot be distinguished reliably using conventional US, cytologic or core biopsy techniques. Unfortunately, the limited evidence available suggests that follicular carcinomas are softer than papillary cancers and overlap in stiffness with benign nodules on USE\(^1\)\(^6\)\(^2\)\(^9\)\(^10\)\(^11\)\(^12\). One recent study using ARFI imaging documented the mean shear wave velocity of 2.01 ± 0.49 m/s for benign nodules, 2.86 ± 0.61 m/s for follicular carcinomas, and 4.11 ± 1.41 m/s for papillary carcinomas\(^1\)\(^2\)\(^9\)\(^10\). This finding is also supported by limited biomechanical data\(^5\)\(^8\)\(^1\)\(^6\)\(^5\). An overlap in stiffness indices between follicular pathologies is unsurprising given that follicular carcinomas and adenomas may exhibit minimal differences pathologically, especially if carcinomas are micro-invasive\(^5\)\(^5\).

Another unresolved question is the accuracy of thyroid USE for malignancy in the presence of diffuse thyroid parenchymal diseases. Background thyroiditis may be expected to reduce the accuracy of strain elastography for malignancy by lowering the relative stiffness of nodules against an abnormally stiffened parenchyma.
A recent study using ARFI imaging documented higher stiffness indices of thyroid parenchyma in Graves’ disease and chronic autoimmune thyroiditis compared with normal parenchyma\[66\]. This postulation needs to be evaluated in future studies although, fortunately, this should not be an issue for quantitative techniques such as SWE, and another study using SWE documented that the elasticity of thyroid nodules was not significantly different in patients with and without coexisting thyroiditis\[67\].

**USE for cervical lymph nodes**

A small number of pilot studies have evaluated USE for detection of malignancy in cervical lymph nodes, with sample sizes ranging from 51 to 141 lymph nodes and comprising a variety of benign and malignant pathologies\[68–76\]. Similar to thyroid USE, there has been marked selection bias as a result of cytologic or histologic verification, resulting in samples comprising a high proportion of malignancies (42–63%). For strain elastography, lymph nodes have been evaluated using either the loose connective tissue surrounding the lymph node or the sternocleidomastoid muscle as reference. In general, metastatic nodes display colour patterns, SRs, or shear wave indices equating to higher stiffness than benign nodes\[68–74\] (Figs. 9, 10). In a recent meta-analysis\[77\] of 9 RTE studies comprising between 50 and 155 cervical or axillary lymph nodes, the pooled sensitivity and specificity for malignancy was 74% (95% confidence interval (CI) 66–81%) and 90% (95% CI 82–94%) using qualitative RTE, and 88% (95% CI 79–93%) and 81% (95% CI 49–95%) using SRs, respectively\[68,71,73,74,76,78–81\]. One of the most promising results was in an early study of 141 peripheral neck lymph nodes evaluated using off-line strain elastography. The study sample included 39 (28%) metastatic nodes from papillary thyroid cancer and 21 (15%) from papillary thyroid cancer.

![Figure 9](image) Longitudinal grayscale US image with corresponding shear wave elastogram showing a reactive lymph node (arrow). The node appears homogeneously blue, with a low mean and maximum SWE stiffness of 8.2 kPa and 14.8 kPa, respectively.
hypopharyngeal squamous cell cancer\textsuperscript{[73]}. An SR >1.5 achieved 85% sensitivity, 98% specificity, and 92% accuracy; while the best grayscale criterion (long-axis to short-axis diameter >2) achieved 75% sensitivity, 81% specificity, and 79% accuracy. However, results of USE studies using off-line processing may not be applicable to real-time USE because the former can potentially produce more reliable elastograms, which reflects the fact that a compromise between computational sophistication/accuracy and speed is required in order to generate elastograms in real time. Tan et al.\textsuperscript{[74]} performed a study evaluating 128 cervical lymph nodes (58 malignant) using RTE, and documented that a strain ratio >1.5 achieved 92.5% sensitivity, 53.4% specificity, and a Youden index of 0.463. By comparison, the best grayscale criterion, long-axis to short-axis diameter >2, achieved 58.6% sensitivity, 70% specificity, and a Youden index of 0.286. More recently, Teng et al.\textsuperscript{[75]} evaluated RTE in 89 cervical lymph nodes (57 malignancies) and documented higher accuracy of SRs (84.3%) compared with qualitative RTE (66.3%) and conventional US (56.2–70.8%).

To account for the possibility of intranodal necrosis in metastatic nodes confounding qualitative RTE, some investigators have modified qualitative scoring systems to classify nodes that display a specific strain pattern, peripheral low strain with central high strain, as suspicious for metastatic infiltration. Alam et al.\textsuperscript{[68]} evaluated 53 metastatic and 32 reactive lymph nodes using a modified classification and reported a sensitivity, specificity, and accuracy of 83%, 100%, and 89% for elastography, 98%, 59%, and 84% for grayscale US, and 92%, 94%, and 93% for combined assessment. Similarly, Ishibashi et al.\textsuperscript{[72]} performed qualitative RTE using a modified classification in 71 cervical lymph nodes (31 metastatic) in patients with oral squamous cell carcinoma, and documented that USE combined with conventional US achieved higher sensitivity (90.3%) and NPV (91.4%) than either modality alone. However, in an early study of qualitative RTE in 74 cervical lymph nodes (37 malignant), Bhatia et al.\textsuperscript{[71]} documented an optimum cut-off of ES >2 achieved only 62.2% sensitivity, 83.8% specificity and 73% accuracy.

Lymph nodes that are only partially infiltrated by tumour may pose a challenge to RTE as scoring systems typically assess strain patterns or SRs with reference to entire nodes. Quantitative USE may overcome this limitation by permitting analysis of specific regions within

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure10.png}
\caption{Transverse grayscale US image with corresponding shear wave elastogram showing a metastatic lymph node from squamous cell carcinoma (arrow). The node appears heterogeneous, with mean and maximum SWE stiffness of 52.4 kPa and 117.6 kPa, respectively.}
\end{figure}
lymph nodes. To date, there has only been one quantitative USE study of cervical lymph nodes. Bhatia et al.\textsuperscript{[70]} evaluated 55 nodes (31 malignant) using SSI and documented that the median stiffness of malignant nodes, 25.0 kPa, (range 6.9–278.9 kPa), was higher than benign nodes (21.4 kPa, 8.9–30.2 kPa) \((P<0.008)\). However, the discrimination of SWE was low as the optimal cut-off (30.2 kPa) attained only 41.9\% sensitivity, 100\% specificity and 61.8\% accuracy.

Overall, the preliminary evidence suggests that USE may be useful to differentiate benign and malignant cervical lymph nodes although further research is required. Ideally, future studies should be sufficiently large and detailed to enable stratification of USE accuracy results according to nodal histology and determine the accuracies of USE for both unselected and selected populations.

**USE for salivary gland lesions**

Several types of salivary pathology have typical sono-graphic appearances although there is considerable overlap\textsuperscript{[82–84]}. Margin irregularity is the main sonographic feature of malignancy but has limited sensitivity and specificity. To date, seven studies have evaluated USE using RTE or SWE for characterization of focal lesions in the major salivary glands\textsuperscript{[85–91]}. Studies samples have ranged from 33 to 74 salivary masses, with between 5 and 18 malignancies from varied pathologies\textsuperscript{[85–91]}. Several studies have documented higher stiffness indices on RTE or SWE for malignancy than benign neoplasms, however, the discriminatory performances of USE are poor. In this regard, several reports suggest that there is appreciable overlap between stiffness of pleomorphic adenomas (PAs) and salivary malignancies\textsuperscript{[85–87,91,92]}. For example, Dumitriu et al.\textsuperscript{[87]} evaluated 74 salivary tumours (18 malignancies) using qualitative RTE and documented higher strain indices in malignant neoplasms compared with benign tumours (mean ES ± SD 2.94 ± 0.87 vs 2.41 ± 0.87), but no difference between malignant neoplasms and PAs, or between PAs and Warthin tumours (WTs). Klintworth et al.\textsuperscript{[89]} evaluated strain pattern distribution on qualitative RTE for 57 parotid tumours

\[\text{Figure 11} \quad \text{Longitudinal grayscale US image with corresponding shear wave elastogram of the parotid gland showing a hypoechoic mass (arrow) that appears relatively homogeneous and low in stiffness. The large region of interest has a low mean and maximum SWE stiffness of 17.1 kPa and 41.8 kPa, respectively. Histology revealed a Warthin tumour.}\]
(8 malignancies) and documented that a pattern of heterogeneous reticular distribution was more frequent in malignant tumours (38%) than in benign tumours (4%). However, no elastographic feature surpassed the accuracy of margin irregularity on grayscale US. Mansour et al.\[^{[90]}\] performed qualitative RTE and ARFI of 33 parotid lesions (4 malignancies) and documented similar strain patterns and ARFI velocities for malignant lesions, WTs, and other benign tumours except for PAs. Bhatia et al.\[^{[85]}\] evaluated 60 focal salivary lesions (5 malignancies) using SSI and documented overlap in elastic moduli between benign pathologies (median stiffness 18.3 kPa, range 0.0–59.4 kPa) and malignant neoplasms (median 13.5 kPa, range 8.0–132.0 kPa), such that there was no clinically useful cut-off (Figs. 11–14). In general, the preliminary data suggest that USE is suboptimal for detection of malignancy in the salivary glands.

\[\text{USE for miscellaneous neck masses.}\]

There are two published preliminary studies that have evaluated the usefulness of USE for characterizing miscellaneous (non-thyroidal, non-nodal, non-salivary) neck masses. Bhatia et al.\[^{[93]}\] performed qualitative RTE for 52 miscellaneous neck masses using a 4-point ES scale. Although there was only one malignant lesion (a metastasis), which had an ES score of 3, 17 (33%) benign lesions had an identical or stiffer pattern on RTE (ES 3 or 4). The same investigators also evaluated 46 miscellaneous neck masses using quantitative SWE, which included six malignant masses, and documented a significantly higher stiffness in malignant lesions (median 226.4 kPa, range 55.6–300.0 kPa) than benign lesions (28.3 kPa, 4.0–300.0 kPa) (Fig. 15). Furthermore, the SWE cut-off with the highest accuracy (174.4 kPa)
achieved 83.3% sensitivity and 97.5% specificity, and the cut-off with 100% sensitivity (55.6 kPa) achieved 75% specificity. Nevertheless, all malignant lesions were suspected on conventional sonography due to their abnormal location (e.g. intramuscular) and suspicious morphological features (e.g. irregular margins, hypervascularity)\(^94\). Consequently, although the accuracy results for SWE were promising, the added value of USE for this indication was questionable.

**Conclusion**

There has been a recent surge in publications evaluating different USE technologies for tissue characterisation, including for detection of malignancy in the head and neck. Most reports document promising accuracies for USE to detect malignancy in the thyroid gland and cervical lymph nodes, although a small but significant number document much less optimistic results. This variation may be attributable to differences between studies in terms of sample selection, elastographic technology, elastographic acquisition and interpretation. Furthermore, most evidence is derived from relatively small studies in selected populations. Consequently, a role for USE in routine sonographic evaluation of the head and neck is unclear at present, although the preliminary evidence provides ample justification for further research in this field. Given the predominantly encouraging results for USE in the head and neck, and the fact that USE technologies are still emerging and continually improving, it is possible that a combination of elastographic and sonographic criteria will become part of routine diagnostic head and neck sonography in the near future.

**Conflict of interest**

The authors have no conflicts of interest to declare.
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Figure 14  Longitudinal grayscale US image with corresponding shear wave elastogram of the parotid gland showing a hypoechoic mass (arrow) that appears relatively homogeneous and low in stiffness, with a large region of interest measuring a mean and maximum SWE stiffness of 20.0 kPa and 36.0 kPa, respectively. Histology revealed a high-grade mucoepidermoid carcinoma. The elastographic appearance resembles that of a Warthin tumour in Figure 11.
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