



Imaging Findings of Granular Cell Tumor of the Breast with Virtual Touch Tissue Imaging Quantification Correlation

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Abstract

In our institution, two cases of granular cell tumor of the breast described in this document were observed. Both share a similar clinical-radiological aspect, very similar to a carcinoma; so, in both cases, the VTIQ study was carried out. In one of the cases, after VTIQ study, the characteristics of malignancy were reinforced, however, the other presented characteristics that diminished its suspect. This difference in behavior can be explained by peculiarities in the histopathological characteristics. Despite the small number of cases, this study may show that the VTIQ was not enough to reduce the suspicion of malignancy in these lesions, with only the biopsy of the lesions remaining the only reliable diagnostic method.

Keywords: Granular Cell Tumor; Tumor Breast; Oncology diagnosis; Innovation; Virtual Touch Tissue Imaging Quantification (VTIQ)

1. Introduction

Only few VTIQ studies applied in the assessment of breast lesions have been reported in the literature. However, in our institution, we have increasingly used this technique to , improve the diagnostic accuracy of ultrasound in the evaluation of breast lesions in an , attempt to avoid unnecessary interventions. We had recently two cases of granular cell , tumor of the breast (GCT), a rare breast tumor, studied with VTIQ. In the literature, the , majority of the studies focus only on the rarity of these lesions and their clinical and , imaging findings with anatomopathological correlation. In this study, in a retrospective , analysis, we evaluate the impact of this technique (VTIQ) in the evaluation of GCT.

2. Case Presentation

2.1 Case 1

A caucasian 40-year-old woman presented to her family doctor with a stiff lump in the upper outer quadrant of the left breast. There were no skin retraction, nipple discharge, or palpable axillary lymph nodes. The patient was referred to our imaging department for further evaluation. On ultrasound study, there was a hypoechoic nodule, with regular borders and posterior acoustic enhancement, with 13 mm of axial diameter on the upper outer quadrant of the left breast (Figure 1). As part of our study, for a greater diagnostic acuity, a VTIQ evaluation of this lesion was performed. It had high values of shear velocity, higher than 3,5 m/s (between 7,4 m/s and 9,8 m/s after three measurements, with an average of all three measurements of 7,5 m/s), comparing with the adjacent tissue this value had an average of 1,6 m/s (Figure 2). Taking into account that for a shear wave velocity ≥ 3.5 m/s the lesion is considered potentially malignant, regardless of the outcome of the quality factor, this increased further the malignancy suspicion of the lesion. An ultrasound guided core biopsy (3 cores), using a 16-gauge needle was done. Histopathological showed a neoplasia containing large eosinophilic and granular cytoplasm with poorly defined limits and a small round central nucleus without atypia. Immunohistochemical findings showed S100 protein diffusely positive, with strong co-expression for CD68 antibody. Negativity for pankeratin AE1 / AE3

and CAM 5.2, negativity for P63 myoepithelial marker (Figure 3a-b). With these findings suggesting benign lesion, the patient had only a conservative surgery and the final diagnostic confirmed a benign granular cell tumour of the breast. The patient did not receive any other treatment, being currently doing annual follow-up, that until now has not shown recurrence or another suspicion.

2.2 Case 2

A caucasian 79-year-old woman presented to her gynecologist with a hard palpable mass in the upper inner quadrant of the breast. There was no skin retraction or nipple discharge, nor were there palpable axillary lymph nodes. In our imaging evaluation, there was a firm mass, a spiculate hypoechoic lesion with slight posterior acoustic shadowing on sonography, measuring 13 mm of axial diameter (Figure 4). These characteristics were suspicious of malignancy. On VTIQ evaluation, unexpectedly, it was a soft lesion with shear velocity values smaller than 3,5 m/s (between 2,6 m/s and 3,1 m/s after three measurements, with an average of all three measurements of 2,9 m/s), comparing with the adjacent tissue this value had an average of 1,3 m/s (Figure 5). So, it had on elastography a lower malignancy rate. However, taking into account that this lesion has mixed high and low quality factors (there are areas with low quality within the mass –yellow areas) and areas of high quality (green), even though shear wave velocity < 3.5 m/s, the lesion is classified as indeterminate and malignancy cannot be excluded. The patient was submitted to ultrasound guided core biopsy (3 cores) using a 14-gauge needle. Histopathological and immunohistochemical findings showed a benign lesion compatible with granular cell tumour of the breast, which was confirmed after a conservative surgery (Figure 6a-b). Currently an annual follow-up is being done.

3. Discussion

Granular cell tumor (GCT) is a rare condition that occasionally affects breast parenchyma, approximately 1:1000 of breast tumors, arising from interlobular breast stroma, representing 5-15% of all GCTs [1]. Although most of the GCTs are benign, <1% of cases, including those of the breasts, are malignant [2].

GCT was first described in the breast by Abrikossoff. Initially, GCT was considered to be a myogenic lesion affecting the breast (myoblastoma). Actually, it is assumed as a tumor originating from perineural or putative Schwann cells of the peripheral nerves or their

precursors that grows in the lobular breast tissue, due to the immunohistochemical features [3].

Although it is a rare entity, we found two recent cases in our institution. It is more common in middle aged, premenopausal, especially African American women and is extremely rare in male patients [3], however our cases occurred in caucasian women and one of them occurred at an old age (79 years old).

It is difficult to identify because it mimics carcinoma clinically and radiologically. Their fibrous consistency and hardness presents as a palpable mass, but painless. This is the reason why it is misdiagnosed that can lead to inappropriate radical treatment resulting in unnecessary physical and psychological hardship [3]. Usually less than 30 mm in size, and are most frequently found in the upper inner quadrant of the breast, in contrast to breast carcinoma, which is more usually located in the upper outer quadrant, corresponding to the cutaneous sensory territory of the supraclavicular nerve [3], although one of our cases had occurred in the upper outer quadrant.

Mammographic appearance of GCT ranges from a round, well-circumscribed mass to an irregular or spiculated lesion. Sometimes, they are associated with skin retraction or skin thickening [1]. They may present variable density, generally without microcalcifications [1]. The same variability can be shown on ultrasound, GCT may manifest as a solid, hypoechoic, poorly marginated mass with marked posterior acoustic shadowing associated to the presence of reactive fibrosis. It could be surrounded by a hyperechoic halo [1], alternatively it may have a benign appearance as a well-circumscribed solid mass, associated with a posterior enhancement depending on the extent of infiltration and degree of reactive fibrosis [4]. In fact, the tumor pathological properties, such as its fibrous consistency and infiltrative growth pattern, are responsible for the malignant imaging appearance [5]. Attending to this fact, the diagnosis has been proved to be exclusively made on pathology.

However, we did not know what kind of lesions these two patients had, and VTIQ study was used to try to improve the diagnostic accuracy. Shear wave elastography is one of the newest developments in ultrasound elastography. Elastography is a method of imaging that permits non-invasive characterization of tissue stiffness [6]. It is based on shear wave velocity information that can be mapped to create an image of the stiffness in the region of interest. Sonoelastography is based on the fact that malignant tumours often alter tissue elasticity [7]. Malignant tissue is firmer than benign tissue. Thus, sonoelastography is used to differentiate benign from malignant lesions. Recently, a two-dimensional (2D) SWE, Virtual Touch

Imaging Quantification (VTIQ, Siemens Medical Solutions, Mountain View, CA, USA) has been introduced to evaluate breast lesions. This technique demonstrates a higher diagnostic performance for breast lesions than conventional ultrasonography [6]. The VTIQ algorithm calculates the velocity of the induced shear waves, which is directly related to tissue stiffness. VTIQ provides four imaging modes: (i) shear wave quality mode includes a 2D color map used to assess the quality measurement of the shear wave speed imaging, which shows colors from high (green) to intermediate (yellow) to low quality (red); (ii) shear wave velocity mode displays colors from high shear wave speed (red) to intermediate (yellow or green) to low (blue); (iii) shear wave travel time mode; and (iv) shear wave displacement mode. To obtain the most optimal and reproducible shear wave speed measurements, the operator should have selected the green areas from the shear wave quality mode in which to place the ROI; areas with liquid or calcification were not allowed to be selected [6].

In our study, each lesion and the fat tissue were measured three times, respectively. Measurements were taken in the area of the maximum velocity. In the same image a shear wave velocity measurement was taken in the surrounding fat tissue, preferably in the same penetration depth of the lesion measurement. The quality map was checked, and green map was tried to be reached in all readings.

A cut-off value established to the shear wave velocity ≥ 3.5 m/s, the lesion is considered potentially malignant, regardless of the outcome of the quality factor, and if a lesion has a complete high quality factor (all green) and a shear wave velocity < 3.5 m/s, the lesion is considered benign, but if a lesion has mixed high and low quality factors and has a shear wave velocity < 3.5 m/s, then the lesion is indeterminate and malignancy cannot be excluded [8].

Based on these principles, it is possible to conclude that VTIQ is not a decision maker to reduce the degree of suspicion of both our lesions. This reinforces the need for biopsy for definitive diagnosis.

Microscopic examination usually reveals an infiltrating growth pattern at the margins of the lesion. The tumor is composed of compact nests or sheets of cells that contain eosinophilic cytoplasmic granules. The cells may be polygonal or elongated, have indistinct cell membranes, but small round nuclei without atypia. The granules are usually prominent and fill the cytoplasm, and they are PAS-positive and diastase-resistant. Nuclei are round to slightly oval with an open chromatin pattern. Variable amounts of collagenous stroma are present. Granular cell tumor is characterized by strong, diffuse immunoreactivity for the S-100 protein, CD 68 and neuron specific endolase but no expression of cytokeratin or the

estrogen and progesterone receptors. Secreted S100 protein is detectable in extra-cytoplasmic area, specific of GCTs [1,9].

To sum up, this benign tumor is only diagnosed by histology and treated by conservative surgery that is local wide resection with caution in evaluating the margins [1]. Complete excision is recommended with tumor-free margins, avoiding local recurrence that has been reported in 2–8% after incomplete excision [3]. The prognosis for benign GCT is excellent [3]. Considering the benign nature of the majority of GCTs, sentinel node biopsy is not indicated in the surgical treatment and no specific adjuvant therapies are suggested; however, long-term follow-up is strongly recommended [1]. Following removal of breast GCTs, patients should be monitored for at least 10 years as distant recurrences have been reported [10].

Figures

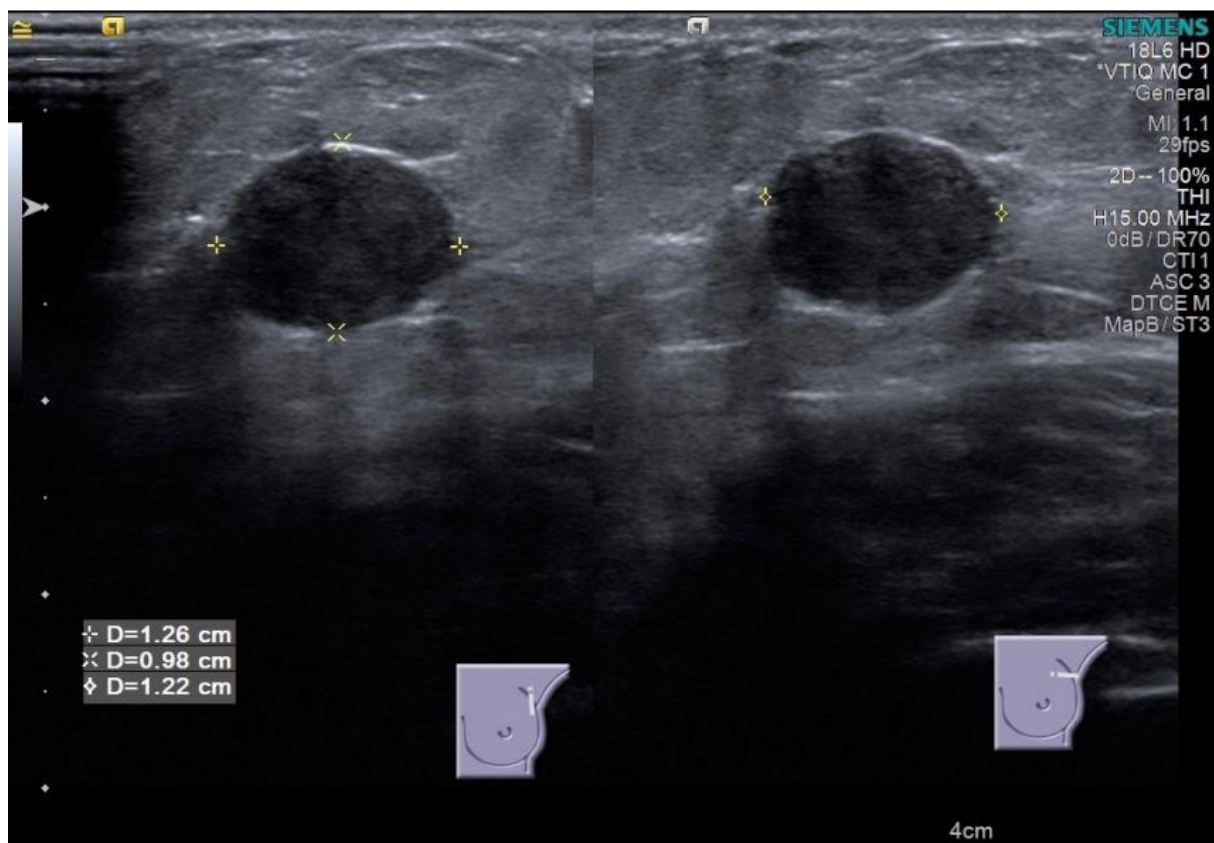


Figure 1: Ultrasound study revealed a hypoechoic nodular, with regular borders lesion and slight posterior acoustic enhancement, with 13 mm, on upper outer quadrant of the left breast.

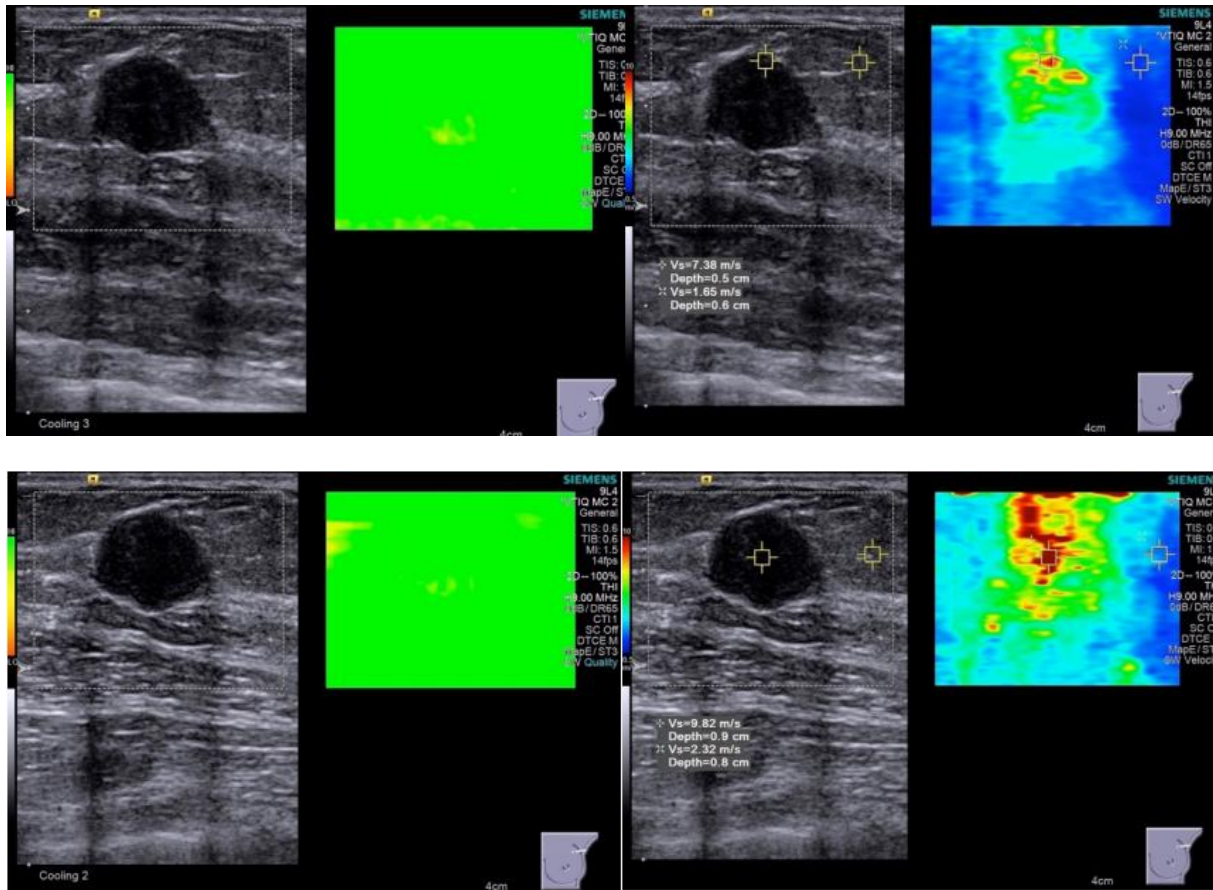


Figure 2: VTIQ evaluation that demonstrate a shear velocity value of higher than 3,5m/s, comparing with the adjacent tissue this value had an average of 1,6m/s.

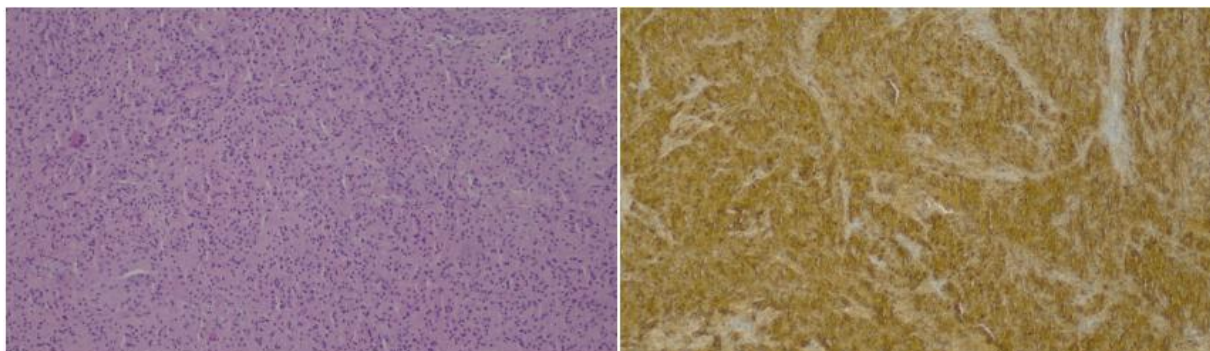


Figure 3: Pathological examination. A lesion containing large eosinophilic and granular cytoplasm with poorly defined limits and a small round central nucleus without atypia (H&E x40). S100 protein immunoreactivity in granular cell tumor (x100).

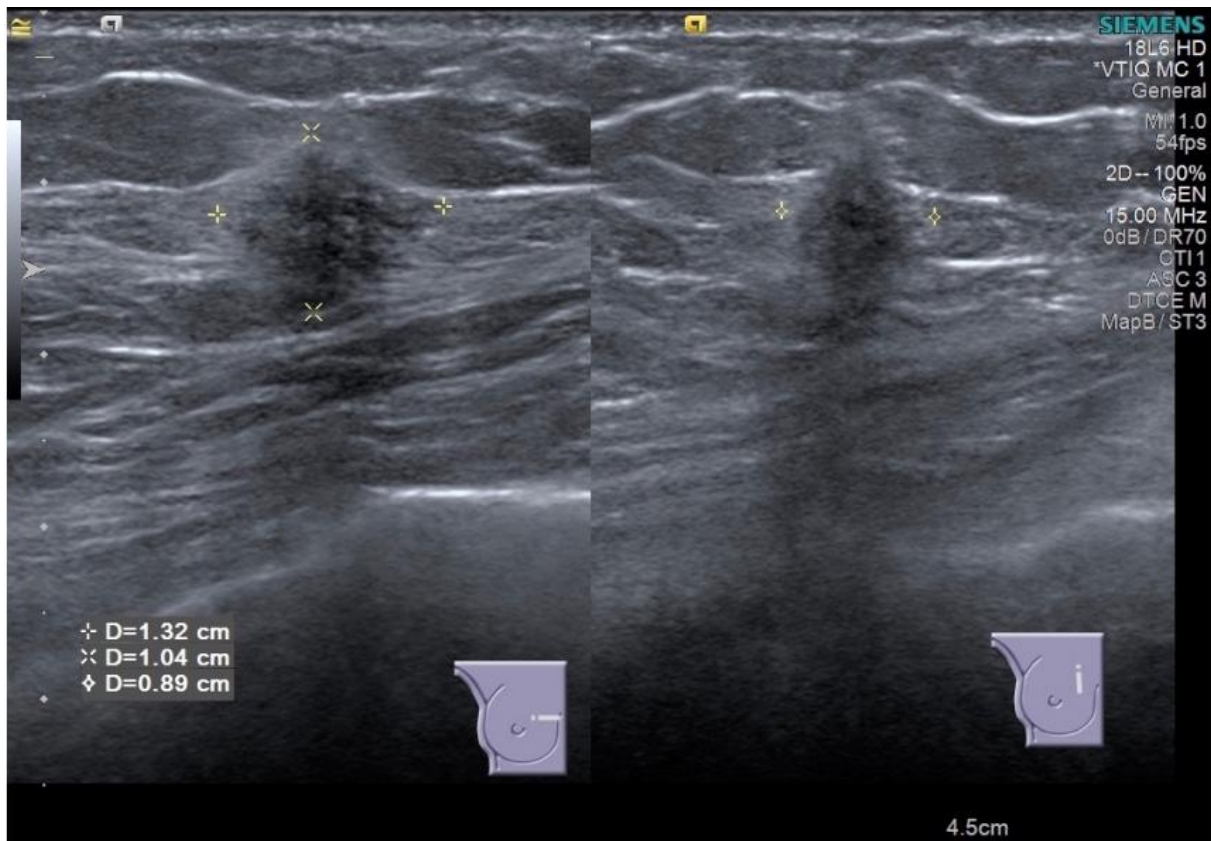
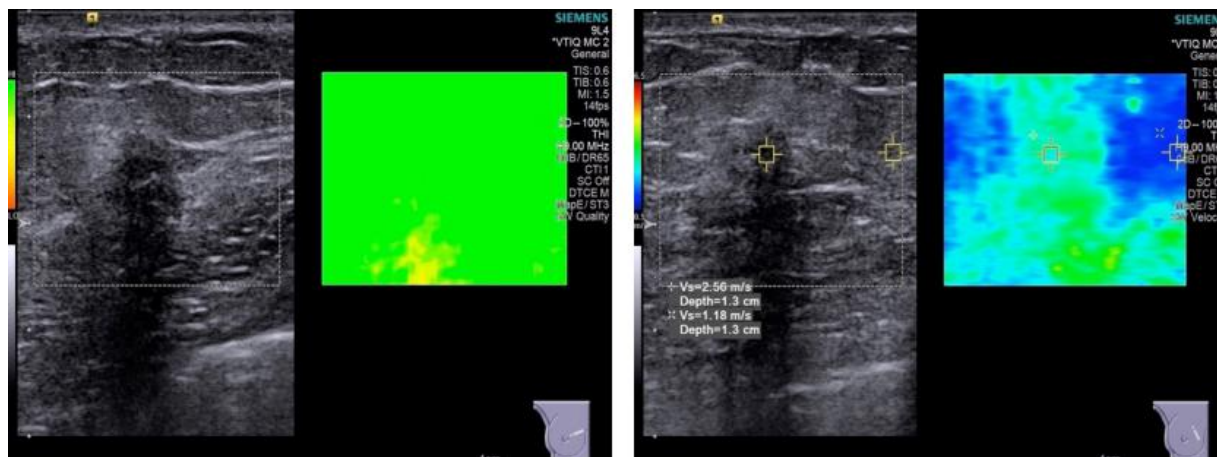


Figure 4: Sonography showed a spiculate hypoechoic nodule, with slight posterior acoustic shadow and it measures 13 mm.



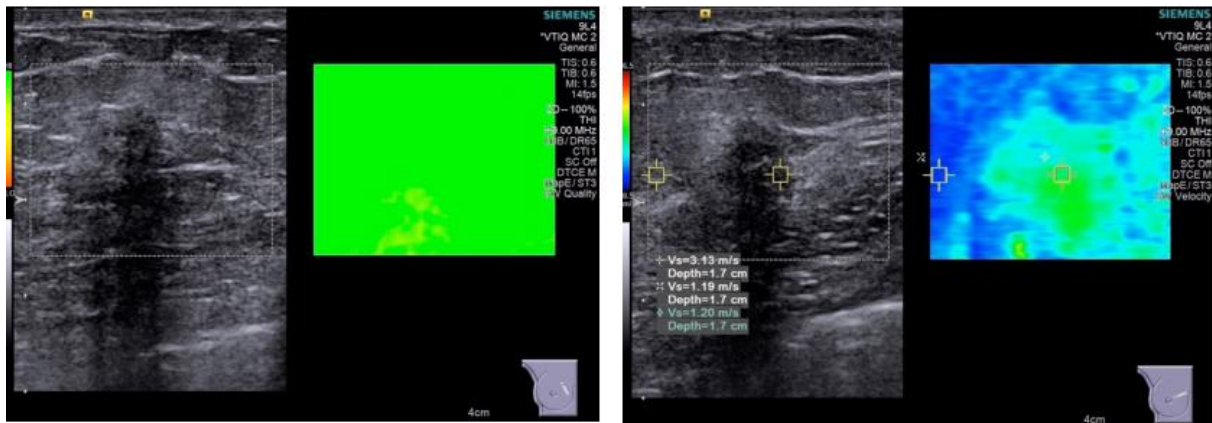


Figure 5: VTIQ evaluation shows a soft lesion with shear velocity value of smaller than 3,5m/s, comparing with the adjacent tissue this value had an average of 1,3m/s.

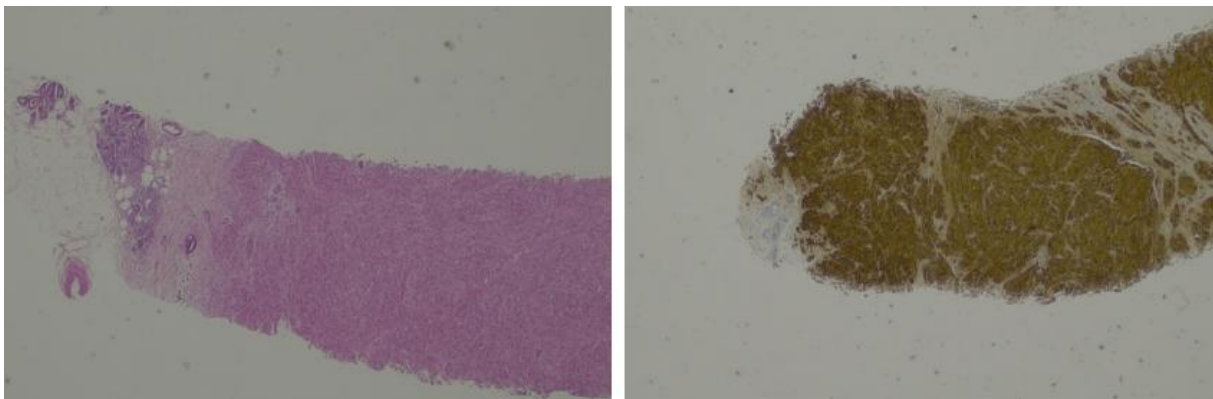


Figure 6: Pathological examination. Granular cell tumor composed of cells with dark small nuclei and granular eosinophilic cytoplasm (H&E x20). S100 protein immunoreactivity in granular cell tumor (x20).

References

- [1] Corso G, Di Nubila B, Ciccia A, et al. Granular cell tumor of the breast: Molecular pathology and clinical management, *The Breast Journal* 2018;1–5. DOI: 10.1111/tbj.13036
- [2] Lara MC, Herrera AM, Cardoso RT, López DL. Granular cell tumor in breast: a case report *Breast Cancer - Targets and Therapy*, 2017;9 245–248 DOI: 10.2147/BCTT.S131446

- [3] Fujiwara K, Maeda I, Mimura H. Granular cell tumor of the breast mimicking malignancy: a case report with a literature review, *Acta Radiol Open*. 2018 Dec; 7(12): 2058460118816537. DOI: 10.1177/2058460118816537
- [4] Yang WT, Edeiken-Monroe B, Sneige N, Fornage BD. Sonographic and mammographic appearances of granular cell tumors of the breast with pathological correlation. *J Clin Ultrasound*, 2006, 34: 153-160. <https://doi.org/10.1002/jcu.20227>
- [5] Adeniran A, Al-Ahmadie H, Mahoney MC, Robinson-Smith TM. Granular cell tumor of the breast: a series of 17 cases and review of the literature. *Breast J*, 2004, 10: 528-531. DOI:10.1111/j.1075-122X.2004.21525.x
- [6] Jia-Wei Sun, Xiao-Lei Wang, Qing Zhao, et al. Virtual touch tissue imaging and quantification (VTIQ) in the evaluation of breast lesions: The associated factors leading to misdiagnosis. *European Journal of Radiology* 110 (2019) 97–104 DOI: <https://doi.org/10.1016/j.ejrad.2018.11.021>
- [7] Frey, H. Realtime elastography. A new ultrasound procedure for the reconstruction of tissue elasticity. *Radiologe*, 2003. 43(10): p. 850-5. DOI:10.1007/s00117-003-0943-2
- [8] Michael Golatta. Evaluation of Virtual Touch Tissue Imaging Quantification (VTIQ - 2D-SWE) in the Assessment of BI-RADS® 3 and 4 lesions: Can patient selection for biopsy be improved? – A confirmatory Multi-Center-Study, by Siemens Medical Solutions Application, Dec. 2015 - Oct 2017. <https://clinicaltrials.gov/ct2/show/NCT02638935>
- [9] J. Huyskens, C. Geniets. Granular Cell Tumor in the Breast Mimicking Breast Carcinoma, *JBR–BTR*, 2014, 97: 289-290. DOI: <http://doi.org/10.5334/jbr-btr.1331>
- [10] Althausen AM, Kowalski DP, Ludwig ME, Curry SL, Greene JF. Granular cell tumors: a new clinically important histologic finding. *Gynecol Oncol*. 2000;77:310-313.