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Ultrasonographic and sonoelastographic features of pleomorphic adenomas of the salivary glands

Dana Dumitriu[1], Sorin M. Dudea[1], Carolina Botar-Jid[1], Grigore Băciuț[2]

[1] University of Medicine and Pharmacy „Iuliu Haţieganu" Cluj-Napoca, Department of Radiology
[2] University of Medicine and Pharmacy „Iuliu Haţieganu" Cluj-Napoca, Department of Oral and Maxillo-Facial Surgery

Abstract

Aims: The typical ultrasound features of pleomorphic adenomas are considered to be the well-defined contour, the regular, sometimes lobulated shape, homogeneous structure and poor vascularization. The goal of our study was to verify the validity of these features and to identify a typical sonoelastographic pattern for pleomorphic adenomas. **Patients and methods:** Between April 2007 and February 2010, 70 salivary gland masses were examined prospectively (58 in the parotid gland, 12 in the submandibular gland). The following features were targeted: size, limits, contour, structure, echogenicity, vascularization, elasticity/stiffness. **Results:** Of the 70 tumors, 32 (45.7%) were pleomorphic adenomas, 12 (17.1%) Warthin tumors, 9 (12.8%) other benign tumors, 13 (18.5%) primary malignant tumors, 3 metastases from carcinoma, and 1 non-Hodgkin lymphoma. Among pleomorphic adenomas, 15 (46.9%) were inhomogeneous, 7 (21.9%) contained necrotic areas and 14 (43.7%) were well-vascularized. The lobulated contour was identified in 14 pleomorphic adenomas (43.7%), no other benign tumor presented this type of contour, but it was identified in 2 malignant tumors (15.3%). On sonoelastography, most pleomorphic adenomas were heterogeneous. The elastic component represented more than 50% of the tumor tissue in 22 cases (68.7%). This aspect was also identified for 6 malignant tumors (46.1%). **Conclusions:** Our results demonstrate that features such as heterogeneous structure, rich vascularization and intra-tumoral necrosis may be identified in a significant number of pleomorphic adenomas. The most specific element in our group was the presence of a lobulated contour, which was not seen in any other benign tumor, but may rarely appear in certain malignant tumors. The elastographic aspect was heterogeneous for most tumors, but the elastic composition identified in most pleomorphic adenomas was also present in a significant proportion of malignant tumors. Therefore, a typical sonoelastographic pattern for pleomorphic adenomas could not be identified.

Keywords: Salivary tumors, pleomorphic adenoma, ultrasound, real-time sonoelastography

Rezumat

Scop: Trăsăturile ecografice considerate tipice pentru adenoamele pleomorfe salivare sunt conturul net, uneori lobulat, structura omogenă si vascularizatia redusă. Scopul studiului nostru a fost acela de a verifica validitatea acestor trăsături si de a identifica un posibil aspect sonoelastografic caracteristic adenoamelor pleomorfe. **Pacienti si metode:** In perioada aprilie 2007 – februarie 2010, 70 de formatiuni tumorale salivare au fost examinate în mod prospectiv (58 localizate în glanda parotidă, iar 12 în glanda submandibulară). Următoarele trăsături au fost urmărite pentru fiecare caz: dimensiuni, delimitare, contur, structură, ecogenitate, vascularizatie, elasticitate. **Rezultate:** Din 70 de tumori, 32 (45.7%) au fost adenoame pleomorfe, 12 (17.1%) tumori Warthin, 9 (12.8%) alte tumori benigne, 13 (18.5%) tumori maligne salivare primare, 3 metastaze ganglionare si un limfom non-Hodgkin. Dintr adenoamele pleomorfe, 15 (46.9%) au prezentat structură inomogenă, 7 (21.9%) au continut arii de necroză, iar 14 (43.7%) au fost bine vascularizate. Conturul lobulat a fost identificat pentru 14 adenoame pleomorfe, nici o altă tumoră benignă nu a mai prezentat acest tip de contur, dar el a fost identificat în 2 tumori maligne (15.3%). La examinarea sonoelastografică, majoritatea adenoamelor pleomorfe au fost heterogene. Componenta elastică a reprezentat mai mult de 50% din compozitia tumorii în 22 de cazuri (68.7%). Acelasi aspect a fost descris si pentru 6 tumori maligne (46.1%). **Concluzii:** Rezultatele obtinute demonstrează faptul că trăsături cum sunt structura heterogenă, vascularizatia bogată sau necroza intra-tumorală pot fi regăsite într-o proportie considerabilă de adenoame pleomorfe. In lotul nostru de studiu, cel mai specific element pentru adenomul plemorf a fost conturul lobulat, care nu a mai fost identificat în nici o altă tumoră benignă, dar poate apărea rar în cazuri de malignitate. Aspectul elastografic a fost heterogen pentru majoritatea tumorilor, iar componenta predominantă elastică identificată în cele mai multe dintre adenoamele pleomorfe a fost prezentă si în aproape jumătate din tumorile maligne. Astfel, nu a putut fi identificat un tipar sonoelastografic caracteristic adenomului pleomorf.

Cuvinte cheie: Tumori salivare, adenom pleomorf, ecografie, sonoelastografie.

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Address for correspondence: Dana Dumitriu
University of Medicine and Pharmacy
„Iuliu Haţieganu" Cluj-Napoca
Emergency County Hospital,
Department of Radiology
Clinicilor 1-3, RO-400006, Cluj-Napoca
Tel: 0264592771/190
Email: danamrc@gmail.com

Introduction

Although tumors of the salivary glands are not common, representing about 3% of all head and neck tumors [1], their differential diagnosis is by no means an easy task, as the histology of this group is very varied, with a large number of both benign and malignant tumors, with a sometimes confusing classification.

Out of this heterogeneous group of tumors, pleomorphic adenomas are the most common, representing 70-

80% of all salivary gland tumors [1,2]. They are most frequently located in the parotid gland and are less common in the submandibular, sublingual and minor salivary glands, which are spread over the floor of the oral cavity.

Numerous studies and attempts have been made in order to obtain a non-invasive imaging method capable of differentiating benign and malignant tumors of the salivary glands. This is of particular importance in the parotid gland, where the surgical approach and thus the risk of injuring the branches of the facial nerve, located in the parotid parenchyma is different depending on the benign of malignant nature of the tumor.

A number of ultrasonographic features are considered typical for pleomorphic adenomas: sharp borders, lobulations of the contour, homogeneous structure, poor vascularization, acoustic enhancement. [3,4] We sought to determine whether or not these features are valid and, furthermore, whether real-time sonoelastography might help in the correct identification of pleomorphic adenomas, by revealing specific features of these tumors.

Patients and methods

Between April 2007 and February 2010, 70 salivary gland masses were examined prospectively in 67 patients, who were directed for ultrasonographic evaluation to the Radiology Clinic - Ultrasonographic Department. Of these patients, 24 (35.8%) were women and 43 (64.2%) were men. The ages of the patients were between 18 and 78 years old (mean age of 50.6 years old). The tumors were all located in major salivary glands: 58 (82.8%) in the parotid and 12 (17.2%) in the submandibular gland. Three patients presented bilateral salivary masses.

Informed consent was obtained from all patients. The study protocol was approved by the local Ethics Commitee.

All patients were examined following the same protocol, using a Hitachi EUB 8500 machine with 8-12 MHz broadband linear transducer. The examination of each patient began with the 2D ultrasound, with measurement of the tumor size in three axes and acquisition of images in two perpendicular planes. The features which were noted on the 2D ultrasound were: tumor size, contour, presence of lobulations, echogenicity, internal structure, presence of calcifications, and presence of acoustic enhancement.

The color Doppler examination was performed afterwards, using the same PRF (pulse repetition frequency) scale settings in all cases and expressing the vascular density as poor or rich, depending on the number of vessels identified. The tumors were considered well vascularized when more than three vessels could be identified and poorly vascularized when only one or two vessels could be identified.

Real-time elastography was performed in all cases, using the same color gain settings and acquiring images in two perpendicular planes with a compression rate of 3 or 4 (on the Hitachi scale). The elastographic box was set at its maximum size, including the mass in question, as well as normal glandular parenchyma, in all cases where this was possible. The sonoelastogram was interpreted qualitatively, the stiffness of the mass was compared with that of the surrounding normal parenchyma and was estimated as superior or inferior to 50% of the total tumoral mass.

The results obtained at ultrasonography (2D, color Doppler, and sonoelasography) were interpreted according to the histopathologic examination performed after surgical resection of the tumors. A 2x2 table was used for the evaluation of the results. The sensitivity, specificity, positive and negative predictive values (PPV, NPV) of the sharp limits, lobulated contour, poor vascularization, homogeneous structure, absence of internal fluid areas, acoustic enhancement, and stiffness < 50% were calculated with a confidence interval of 95%.

Results

The histopathology diagnoses of the tumors included in our group are presented in table I.

The majority of the tumors were pleomorphic adenomas, Warthin tumors and malignant tumors. The ultrasonographic features of these tumors are detailed and compared in table II.

The sensitivity, specificity, PPV, NPV of the sharp limits, lobulated contour, poor vascularization, homogeneous structure, absence of internal fluid areas, acoustic

Table I. The histopathology diagnosis of the 70 salivary gland masses in the study group.

Tumor type	Number	Percentage
Pleomorphic adenoma	32	45.7 %
Warthin tumor	12	17.1%
Other benign tumors	9	12.8%
Myoepithelioma	1	
Oncocytoma	1	
Neurofibroma	1	
Dermoid cyst	2	
Branchial cyst	2	
Lipoma	1	
Benign lymphoepithelial lesion	1	
Malignant tumors	17	24.2%
Primary	13	18.5%
Secondary	4	

Table II. Ultrasound and sonoelastographic features of pleomorphic adenomas, in comparison with Warthin tumors and primary malignant tumors.

	Pleomorphic adenoma (n=32)	Warthin tumor (n=12)	Primary malignant tumors (n=13)
	Number (%)	Number (%)	Number (%)
Mean size (mm)	27.3	28.8	35.05
Location			
Parotid	28 (87.5%)	12 (100%)	8 (61.5%)
Submandibular	4 (12.5%)	0	5 (38.5%)
Limits			
Well defined	30 (93.7%)	12 (100%)	4 (30.7%)
Poorly defined	2 (6.7%)	0	9 (69.3%)
Lobulated contour			
Yes	14 (43.7%)	0	2 (15.3%)
No	18 (56.3%)	12 (100%)	11 (84.7%)
Internal structure			
Homogeneous	17 (53.1%)	3 (25%)	6 (46.1%)
Heterogeneous	15 (46.9%)	9 (75%)	7 (53.9%)
Liquid areas			
Yes	7 (21.9%)	8(66.6%)	3 (23%)
No	25 (78.1%)	4 (33.3%)	10 (77%)
Calcifications			
Yes	0	0	4(30.7%)
No	32 (100%)	12 (100%)	9 (69.3%)
Acoustic enhancement			
Yes	28 (87.5%)	11 (91.6%)	4 (30.7%)
No	4 (12.5%)	1 (8.3%)	9 (69.3%)
Vascularization			
Well vascularized	14(43.7%)	7(58.3%)	9(69.3%)
Poorly vascularized	18(56.3%)	5(41.7%)	4(30.7%)
Elastographic structure			
Stiffness area< 50%	22(68.7%)	7(58.3%)	6(46.1%)
Stiffness area > 50%	10(31.3%)	5(41.7%)	7(53.9%)

enhancement, and stiffness < 50% in these three types of tumors are presented in table III.

Figures 1 through 8 illustrate some of the cases in this study group. Their features are reviewed in detail in the "Discussion" section, along with comments for each specific feature.

Table III. Sensitivity, specificity, positive and negative predictive value for ultrasound features of pleomorphic adenoma.

Ultrasound feature n=32	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Sharp limits	93.7	36	65.2	81.8
Lobulated contour	43.7	92	87.5	56.0
Homogeneous structure	53.1	64	65.3	51.6
Absence of fluid areas	78.1	44	64.1	61.1
Poor vascularization	56.2	64	66.6	53.3
Acoustic enhancement	87.5	40	65.1	71.4
Stiffness < 50%	68.7	48	62.8	54.5

n – number of tumors, PPV – positive predictive value, NPV – negative predictive value

Discussion

The effort to provide a solid pre-operative differential diagnosis of salivary gland tumors in order to achieve a more precise planning of the surgical intervention which is the treatment for almost all of these masses, has so far been disappointing. Because pleomorphic adenomas are the most common salivary masses, representing 70-80% of all salivary masses, their features are the best known, however the mixture of cellular types in the internal structure of pleomorphic adenomas (also known as benign mixed tumors) means that the gross imaging features will also sometimes be very different from the common pattern.

A large number of studies are available, trying to identify the most characteristic features for each type of tumor and, mostly, to differentiate between benign and malignant tumors. Grayscale ultrasound, color and spectral Doppler, CT and MRI have been employed in this pursuit [3,5-13]. However, the differential diagnosis is not easy, since there is considerable overlapping of internal structure, patterns of vascularization and enhancement between benign and malignant tumors.

A number of specific features have been identified by the authors of these studies for pleomorphic adenomas. Most authors describe pleomorphic adenomas as well-defined, sometimes lobulated, sometimes presenting a peripheral capsule. The structure is described as mostly homogeneous, solid, sometimes with calcifications and the vascularization is poor [4].

Our main purpose was to verify whether these widely accepted features are valid and, furthermore, to identify what key features might help us to tell pleomorphic adenomas apart from other benign and malignant tumors.

In our group, most pleomorphic adenomas were located in the parotid gland (87.5 %). They represented 48.2% of all masses located in the parotid, which is less than the 80% usually reported [1]. Four pleomorphic adenomas were located in the submandibular gland, representing 33.3% of all masses in this location. By comparison, 5 of 12 submandibular masses (41.6%) were malignant and only 8 of 58 parotid masses (13.7%) were malignant. This is in accordance with commonly reported malignancy rates, as it is a well-known fact that the rate of malignancy is higher in the smaller salivary glands and it is highest in the minor salivary glands [1].

As expected, most pleomorphic adenomas were well-defined, with sharp borders (fig 1a). This was also true for Warthin tumors, which were all very well defined. Although most malignant tumors did have poorly-defined borders, a considerable proportion of them (30.4%) demonstrated sharp, well-defined borders. A particularly interesting and useful feature was the presence of a lobulated contour (fig 1b): although only about half of pleomorphic adenomas demonstrated lobulations, this feature was not present in any other benign tumor and it was identified in only two malignant tumors; these malignant masses were also sharply limited, which made the diagnosis very difficult. Although the presence of lobulations was not a very sensitive sign (43.7%), our study showed that it had high specificity for pleomorphic adenomas (92%). Some reports state that a lobulated contour is present especially in larger pleomorphic adenomas [14]. Despite this, we found that the mean size of lobulated and of non-lobulated pleomorphic adenomas were very close (29.8 mm vs. 30.7 mm).

The homogeneity of the tumors seems to have no relevance for the differential diagnosis: about half of pleomorphic adenomas and malignant tumors had a heterogeneous structure (fig 2). Contrary to other literature reports [4,14], we did not find calcifications in any of the pleomorphic adenomas. Instead we found microcalcifications in 30.7% of malignant tumors (specificity 100%, PPV 100%, sensitivity 30.7%, NPV 83%) (fig 3b). In order to validate this observation a larger numbers of ultrasonographic examined tumors is needed, as malignant tumors only represented 18.5% of he masses in this study group.

Most literature reports consider that internal liquid areas are specific for Warthin tumors (fig 3c), but possible also in pleomorphic adenomas, schwannomas and malignant tumors [4]. In our group internal fluid areas were present mostly in Warthin tumors (66.6%), but we also found fluid areas in 21.9% of pleomorphic adenomas (fig 2c, d) and 23% of malignant tumors. These fluid areas were more extensive, and with a regular contour in Warthin tumors, whereas in pleomorphic adenomas (in very large masses) they were of smaller size, with irregular contour, suggestive of areas of necrosis. Our study showed that the presence of liquid areas inside a salivary mass, especially with irregular outline, does not exclude the diagnosis of pleomorphic adenoma.

Acoustic enhancement was present in most pleomorphic adenomas (87.5%) (fig 1a, fig 2) and Warthin tumors (91.6%) (fig 3c), reflecting not only the presence of liquid content, but also the relative homogeneity of these masses, in terms of internal echoes. Of the 15 tumors without acoustic enhancement, 9 were malignant (fig 3d), which means that, in combination with other features, the presence of acoustic enhancement can be a sensitive sign for pleomorphic adenomas and other benign masses (sensitivity 87.5%, specificity 40% for pleomorphic adenoma; sensitivity 88.6%, specificity 69.2% for a benign mass). Based on our results, since only 5 benign masses lacked acoustic enhancement, the absence of this sign can lead to the suspicion of malignancy with a specificity of 88.6% and a PPV of 100%.

The common belief, and the basis for all vascular studies of salivary gland masses, is that malignant tumors are better vascularized and have a different vascularization pattern from benign tumors [4,5,9]. Our study does not confirm this statement. Furthermore, it contradicts the commonly presented pattern for pleomorphic adenoma: in our study group, the number of well-vascularized and poorly-vascularized pleomorphic adenomas was almost equal (43.7% vs. 56.3%) (fig 4). A larger proportion of malignant tumors (69.3%) presented a rich vascularization, but 30.7% of them were poorly vascularized.

One of the goals of this research was to determine whether real-time sonoelastography might reveal a certain pattern of pleomorphic adenomas, either by the extent of the elastic and stiff areas or by the distribution of these areas. Although most pleomorphic adenomas were predominantly elastic (68.7%) (fig 6b), we found the same aspect in 46.1% of malignancies. An almost complete stiffness (fig 6a), as well as a mixed pattern with predominant stiffness (fig 6b) was seen in 31.3% of pleomorphic adenomas. In stiff malignant tumors, the most rigid areas seemed to be located centrally (fig 7a, fig 8c), but this was also seen in some pleomorphic adenomas. The presence of liquid areas made the evaluation of the elasticity of the solid areas difficult, by producing the typical color stratification pattern (blue-green-red) [15] (fig 6d, fig 8b). This artifact could also be useful in identifying small fluid areas, in cases where they are not apparent on the 2D ultrasound, or in distinguishing between a very hypoechoic solid mass and a cyst.

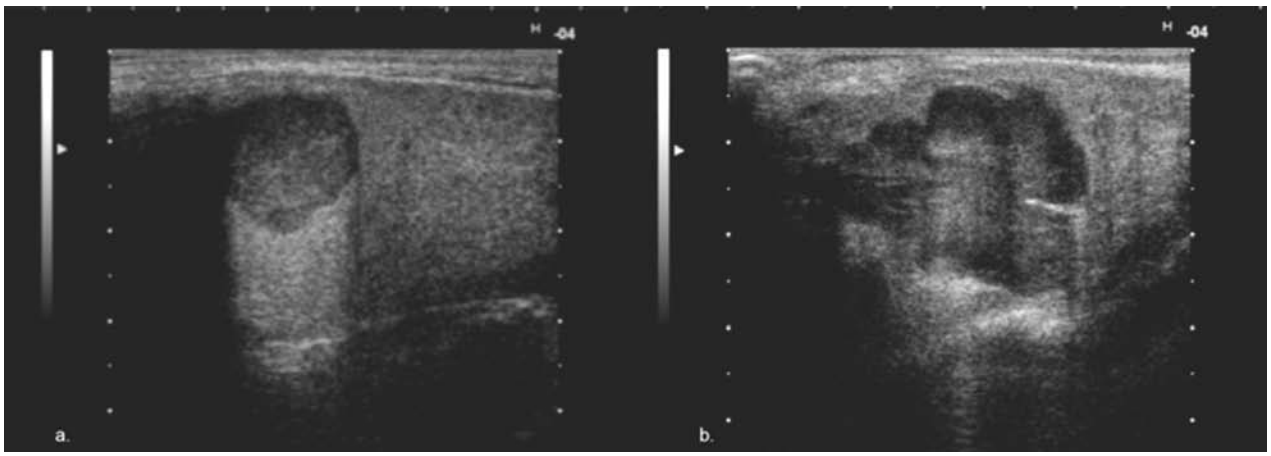


Fig. 1. Grayscale ultrasound: Pleomorphic adenoma – types of contour; a) Small superficial parotid mass – regular contour; b) Lobulated, well-defined contour.

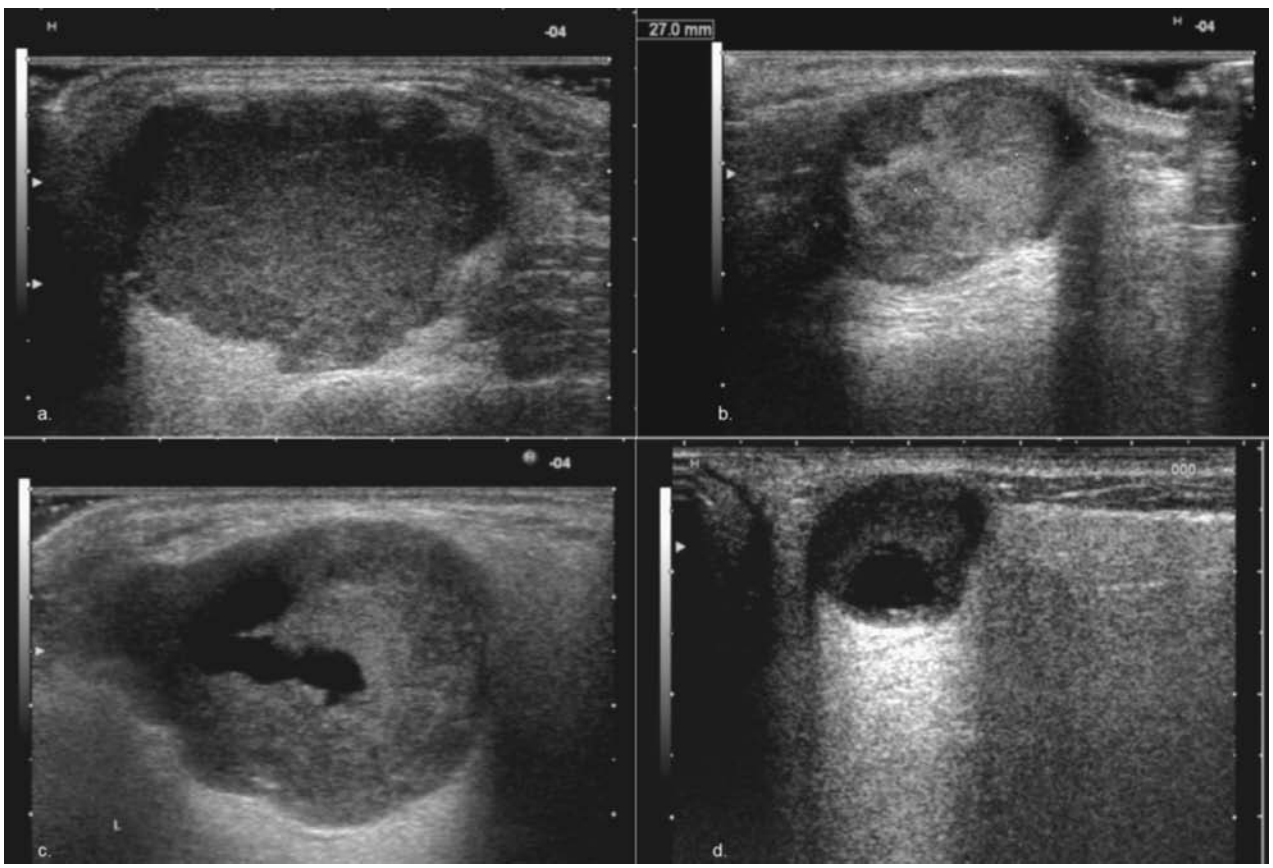


Fig. 2. Grayscale ultrasound: Pleomorphic adenoma – internal structure; a) Large, slightly lobulated homogeneous mass; b) Heterogeneous internal structures, with areas of different echogenicity, without calcifications or necrosis; c) Large mass with internal fluid (necrotic) areas; d) Small superficial mass with an internal necrotic area.

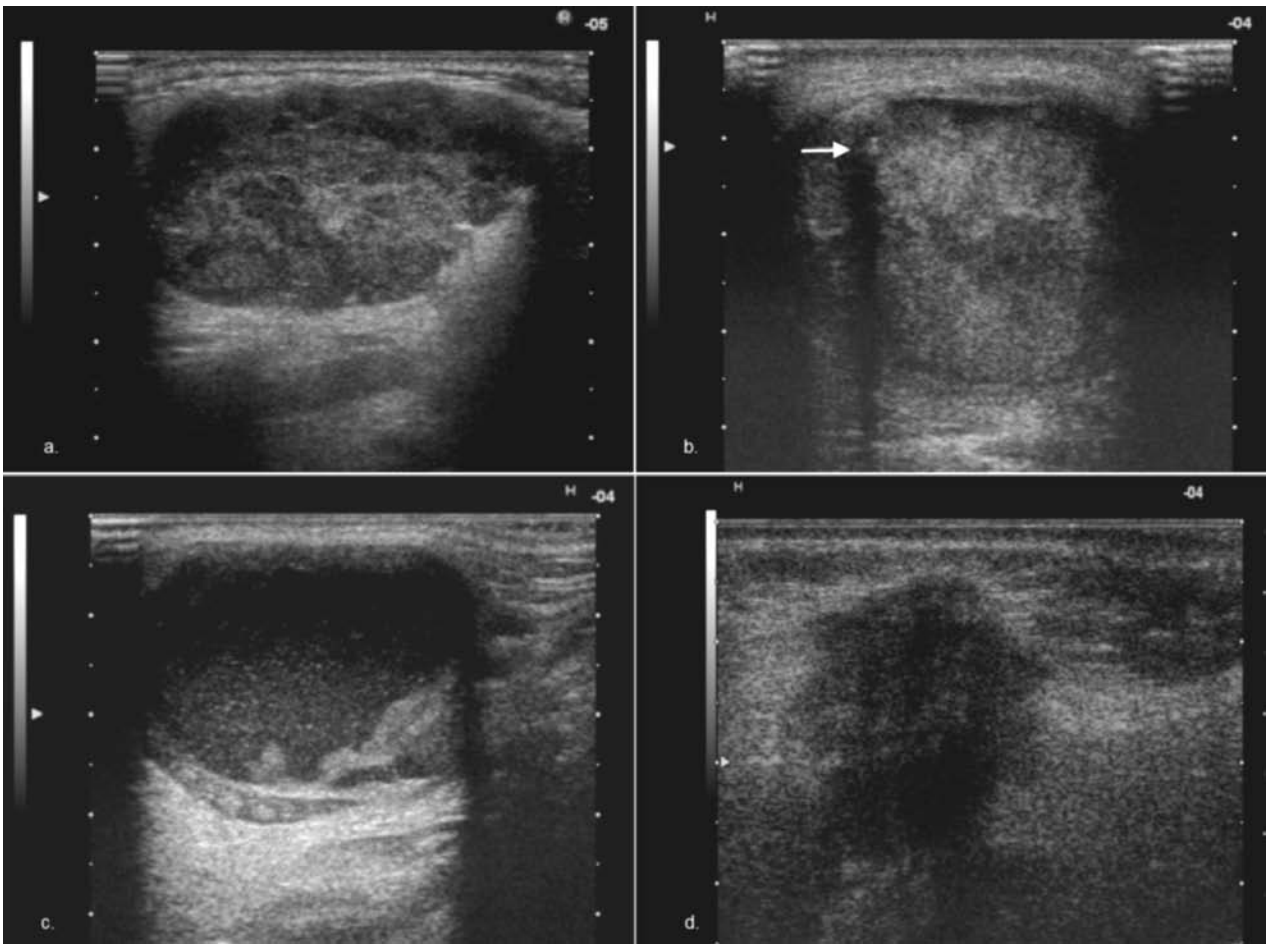


Fig. 3. Grayscale ultrasound: Internal structure of different salivary gland masses; a) Pleomorphic adenoma: heterogeneous internal structure without necrosis or calcification; b) Malignant tumor (squamous cell carcinoma): isoechoic, slightly heterogeneous mass, with a small area of calcification with acoustic shadowing (arrow); c) Warthin tumor: well-defined mass with large fluid areas; d) Malignant tumor (adenocarcinoma): typical hypoechoic, ill-delimitated mass, without acoustic enhancement.

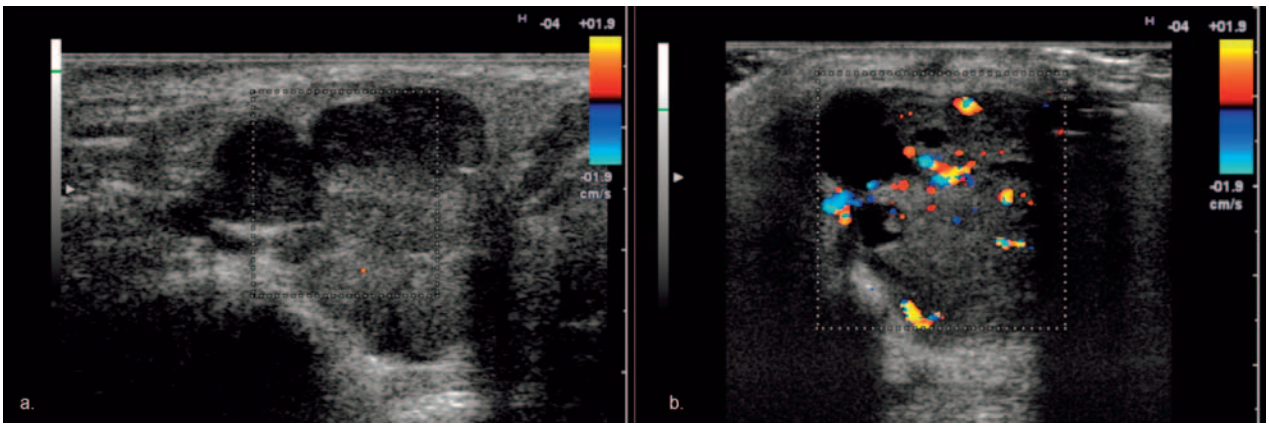


Fig. 4. Color Doppler ultrasound – pleomorphic adenoma; a) Typical hypovascular lobulated mass; b) Rich vascularization in an inhomogeneous mass with necrotic areas.

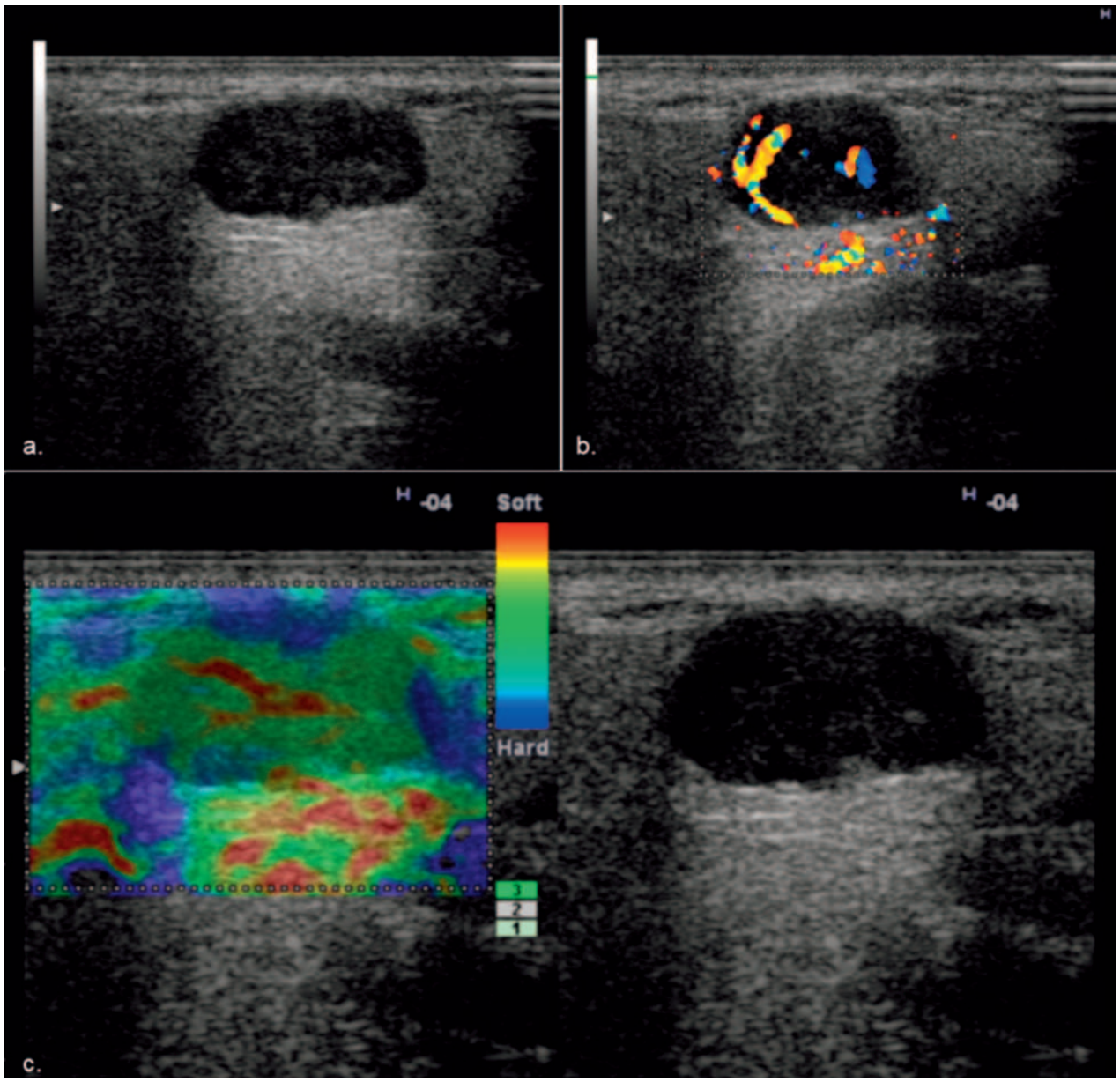


Fig. 5. Pleomorphic adenoma; a) Grayscale ultrasound: small, hypoechoic, homogeneous mass with acoustic enhancement; b) Color Doppler ultrasound: rich vascularization; c) Sonoelastography: predominantly elastic structure, similar to normal parotid parenchyma.

Because benign salivary gland masses, such as pleomorphic adenomas, can have an important fibrous, stiff component, sonoelastography does not seem to be able to bring something new to the differential diagnosis between benign and malignant masses. In cases where the grayscale ultrasound was difficult to interpret, it did not help us to clarify the differential diagnosis (fig 7). As most masses are a mixture of stiffness and elasticity in different proportions, the main benefit we derived from elastography was that of confirming necrotic areas in cases where they were too small to be correctly identified on grayscale ultrasound – however, as presented above, the presence of necrotic areas alone is not a specific element for any kind of tumor and should not be used to exclude a pleomorphic adenoma.

On the performance of elastography, we could only confront our results with that of one other published study, conducted by Bathia et al [16] which compared focal sali-

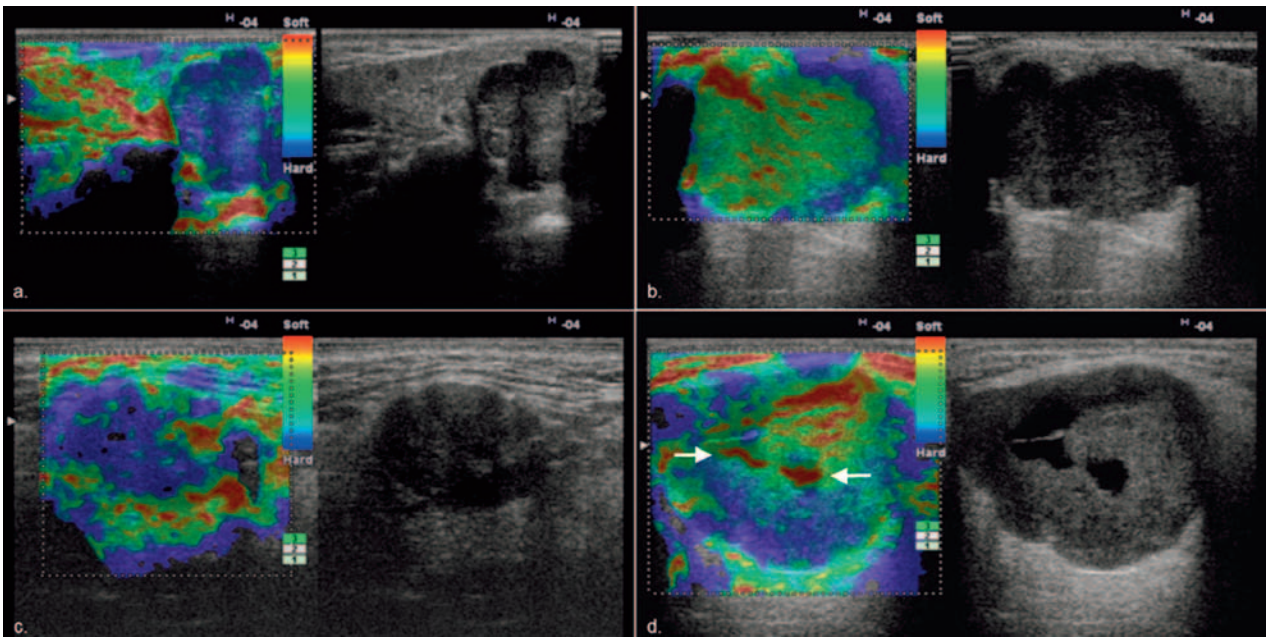


Fig. 6. Sonoelastography: pleomorphic adenoma; a) The typical, lobulated mass (same as in fig. 1b) is almost entirely stiff; b) Large lobulated mass with mostly elastic structure; c) Submandibular mass presenting a mosaic pattern of elasticity and stiffness; d) Large mass with necrotic areas: the solid segments are mostly stiff, the fluid areas produce the color stratification artefact – BGR (arrows).

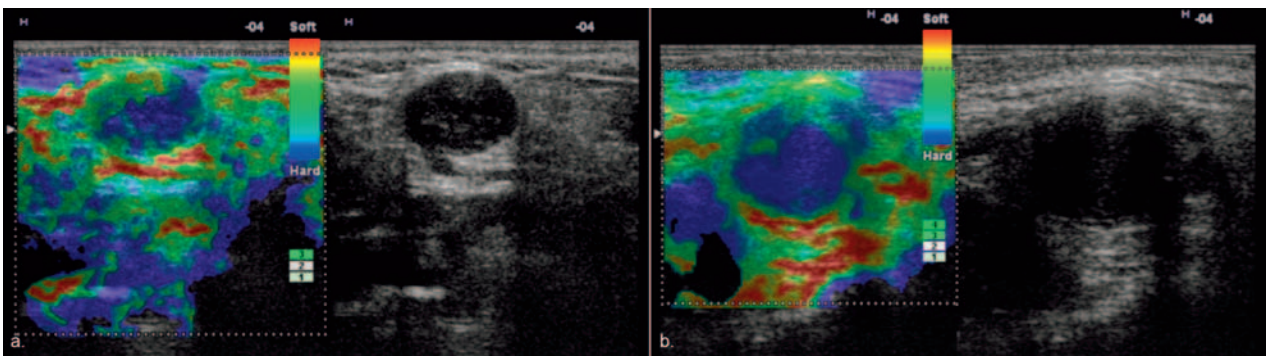


Fig. 7. The differential diagnosis in ultrasound and elastography can sometimes be difficult: a) Metastatic lymph node at the lower pole of the parotid gland; b) Small stiff pleomorphic adenoma in the lower pole of the parotid gland.

vary lesions in terms of relative stiffness and concluded that sonoelastography seems to have little benefit in the benign-malignant differential diagnosis in salivary gland tumors.

The results obtained on our group of patients indicate that the differential diagnosis between the many types of salivary gland masses does not benefit from sonoelastography, since it has a limited way of representing very different histological structures. These observations have to be validated on a larger number of patients and a wider variety of masses, since the number of tumors other than pleomorphic adenomas in this group was too low to allow a solid statistic interpretation of the results. Although it reflects the true distribution of salivary masses, this is in fact the main limitation of the study – the small number of tumors other than pleomorphic adenoma. A quantitative, rather than qualitative estimation of elasticity/stiffness would provide a more objective comparison between the different types of tumors.

Conclusions

Our study shows that the ultrasound investigation of pleomorphic adenomas can be challenging: the most specific feature is a lobulated, well-defined contour. In the absence of this, neither the internal structure, nor the vascularization or the sonoelastographic aspect can identify a pleomorphic adenoma for certain.

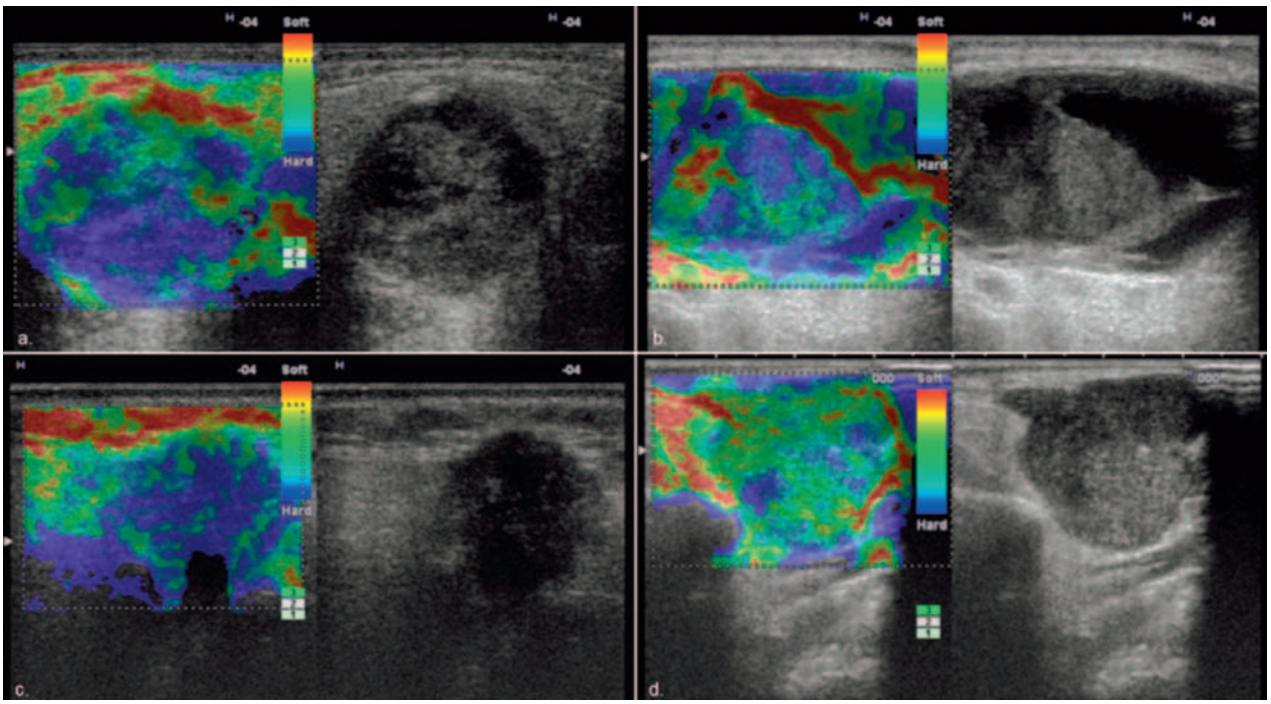


Fig. 8. Sonoelastography: a) Pleomorphic adenoma: mixed aspect, with predominant stiffness; b) Warthin tumor: stiff solid areas, large fluid areas with color stratification artefact; c) Malignant tumor (adenocarcinoma): the same case as in fig. 3d – on elastography the mass appears predominantly stiff; d) Malignant tumor (basal cell carcinoma) – deceiving ultrasound and elastographic aspect, with well-defined borders and predominant elasticity.

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