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RESEARCH

Pleomorphic adenoma of parotid gland: delayed enhancement on computed tomography

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Objectives: To assess the efficacy of multiphasic CT with 8 min delayed acquisition in the differential diagnosis between pleomorphic adenomas and other parotid neoplasias.
Methods: Between January 2004 and April 2007, 62 patients with parotid enlargement were enrolled in this prospective study. The CT protocol applied included the following four acquisitions: without contrast medium and 30 s, 120 s and 8 min after intravenous injection of contrast medium. We considered the degree of the enhancement of the lesions (rated as "low", "moderate" and "strong") and the degree of enhancement homogeneity (rated as "not homogeneous", "mildly homogeneous" and "uniform"). These parameters were compared with Hounsfield values of the lesions computed in each phase. The diagnosis was confirmed in all patients after surgery.
Results: On histological examination, 36 tumours were classified as pleomorphic adenomas and 26 as non-pleomorphic adenomas. On the basis of a statistical comparison, the third phase proved to be the most effective in the differential diagnosis between pleomorphic adenoma and non-pleomorphic adenomas, both for the assessment of the degree of the enhancement (in this phase, strong enhancement showed a sensitivity of 61.11%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 53.33%) and, above all, for the homogeneity of the enhancement (in this phase, indeed, uniform enhancement showed sensitivity, specificity, PPV and NPV of 100%).
Conclusions: Our results seem to indicate that multiphasic CT with 8 min delayed acquisition allows the differential diagnosis between pleomorphic adenomas and other parotid neoplasias.
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Keywords: adenoma, parotid, computed tomography, pleomorphic

Introduction

Pleomorphic adenoma is the most common tumour of the salivary glands. Due to its benign nature, surgeons can perform minimally invasive surgery.[1,2]

The differential diagnosis with other forms of neoplasia, such as carcinomas, Warthin's tumours and metastasis, is necessary to determine the best therapeutic approach, since different pathologies require different therapies.[3,4]

Today, multislice CT is one of the primary imaging modalities used to assess tumours of the salivary glands. It allows the detection of lesions and assessment of their extension and characteristics as well as their relationships to nearby structures.[5–7]

However, this technique has some limitations linked to the pathological classification of the tumour. In relation to this, higher accuracy levels might be obtained through a multiphasic acquisition with an 8 min delayed phase after contrast administration.

The aim of this study was to assess the efficacy of multiphasic CT with the 8 min delayed acquisition in the evaluation of the enlargement of salivary glands and, in particular, in the differential diagnosis between pleomorphic adenomas and other parotid lesions.

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Materials and methods

During a period of 3 years (January 2004 to April 2007) 62 patients (28 women and 34 men; with age range 25–80 years and mean age 50) with clinically tested parotid enlargement underwent CT examination.

The histopathological diagnosis was confirmed in all patients after surgery or ''open sky'' biopsy. Examinations were carried out with the four-layer Philips CT. The technical protocol applied to all of the examinations included the following four acquisitions: (a) without contrast medium; (b) in the early phase, 30 s after intravenous injection of non-ionic contrast material (90 ml) at 3 ml s^{-1}; (c) a delayed scan (120 s scan delay); (d) a further delayed phase, after 8 min.

Pre-contrast and early scans targeted the skull base, going through the superior thoracic outlet with the following parameters: 35 s acquisition time, 3 mm collimation and 3 mm s^{-1} table feed. To increase radiation protection, the volume acquisition was reduced to the area of the lesion in the last two phases.

The total radiation dose received by the patients was not higher than the amount received during traditional biphasic techniques without reduction of the volume acquisition. Written informed consent was obtained before each examination, to meet transparency needs.

Each CT scan was assessed by three experienced radiologists who were blinded to the histological results. Each radiologist evaluated the results autonomously and assessed, for each phase, the degree and homogeneity of the enhancement of the lesion.

The degree of the enhancement was rated as ''low'', ''moderate'' or ''strong'', while the degree of homogeneity was rated as ''not homogeneous'', ''mildly homogeneous'' or ''uniform''.

Each lesion's Hounsfield value (HU) was determined in each phase, computed by drawing a region of interest (ROI) around the entire area (7–32 mm^2).

Wide ROIs were used, avoiding cystic and necrotic areas which are frequently present in benign and malignant parotid lesions.

This is necessary during the subjective assessment of the degree and homogeneity of the enhancement of the lesions because the presence of cystic and necrotic areas can modify the homogeneity of enhancement of solid areas.

From this point of view, a lesion with a ''not homogeneous'' density may also have a homogeneous enhancement.

Lesions with Hounsfield values under 70 HU were rated as having a ''low'' degree of enhancement; a ''moderate'' degree ranged between 70 HU and 90 HU and a ''strong'' degree was above 90 HU.

At the end, the statistical significance of the most common degree and homogeneity patterns of the enhancement of pleomorphic adenoma during each phase were compared to determine the most useful post-contrast phase in the differential diagnosis between pleomorphic adenoma and other parotid lesions (cited in the text as ''non-pleomorphic adenoma'').

Results

Out of 62 histologically confirmed parotid tumours, 36 were pleomorphic adenomas, 15 Warthin's tumours, 5 squamous cell carcinomas, 3 mucoepidermoid tumours and 3 acinic cell carcinomas.

The maximum transversal diameter of the lesions ranged from 10 mm to 50 mm (average 24 mm); no statistically significant differences were detected among the various histological tumour types in relation to dimension.

In all three phases, the radiologists obtained the same results both for degree and for homogeneity of the enhancement.

Results related to degree, homogeneity of enhancement and HU values in each phase are summarized in Table 1.

As to the degree of enhancement, the most sensitive pattern of pleomorphic adenoma in the first post-contrast phase was low enhancement (25 out of 36 pleomorphic adenomas), also detected in 4 out of 26 non-pleomorphic adenomas (all malignant lesions).

In the second post-contrast phase, the most common pattern of pleomorphic adenoma was moderate enhancement (22 out of 36); this was detected in 9 of 26 non-pleomorphic adenomas in the same phase.

In the third post-contrast phase, the most common pattern of pleomorphic adenoma was strong enhancement (22 of 36); in this phase, it was not detected in non-pleomorphic adenomas.

With respect to the homogeneity of the enhancement, the most common pattern of pleomorphic adenoma in the first post-contrast phase was the ''not homogeneous'' (28 of 36), detected also in 5 of 26 non-pleomorphic adenomas.

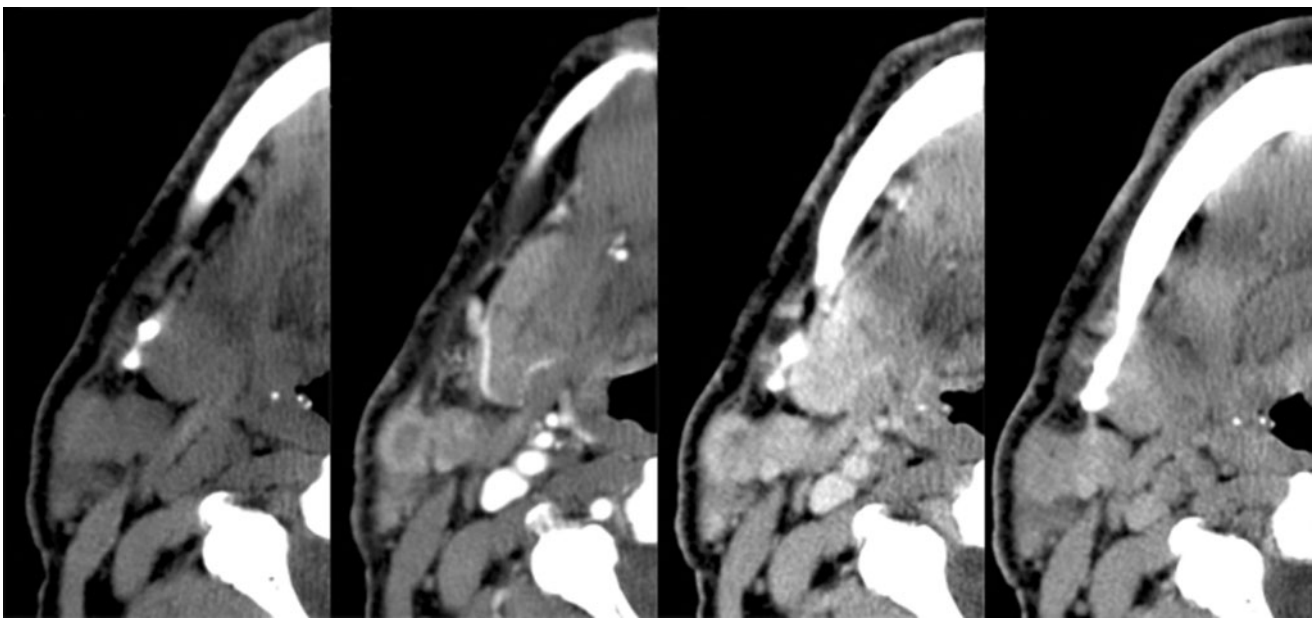
In the second post-contrast phase, the most common pattern of pleomorphic adenoma was, again, the ''not homogeneous'' phase (19 of 36), also detected in 8 out of 26 non-pleomorphic adenomas.

In the third post-contrast phase, all pleomorphic adenomas showed a uniform enhancement (36 of 36); this pattern was not detected in non-pleomorphic adenomas.

These patterns were the most significant for each post-contrast phase for the differential diagnosis between pleomorphic adenomas and non-pleomorphic adenomas (Figures 1–3). On the basis of a statistical comparison, the third phase proved to be the most effective both for the assessment of the degree of the enhancement (in this phase strong enhancement showed sensitivity of 61.11%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 53.33%; see Table 2) and, above all, for the homogeneity of the enhancement (in the third phase, indeed, uniform enhancement showed

Table 1 Different behaviour of enhancement among the histological types of parotid enlargements

		Degree			*Homogeneity*		
Histology	*Phase*	*Low <70 HU*	*Moderate 70–90 HU*	*Strong >90 HU*	*Not homogeneous*	*Mildly homogeneous*	*Uniform*
Pleomorphic	Early	25 (69.4%)	11 (30.6%)	0	28 (77.8%)	8 (22.2%)	0
adenoma	Delayed 1	15 (41.7%)	21 (58.3%)	0	19 (52.8%)	17 (47.2%)	0
($n = 36$)	Delayed 2	0	14 (38.9%)	22 (61.1%)	0	0	36 (100%)
Warthin's	Early	0	7 (46.6%)	8 (53.4%)	2 (13.4%)	8 (53.3%)	5 (33.3%)
tumours	Delayed 1	8 (53.3%)	6 (40.0%)	1 (6.7%)	6 (40.0%)	8 (53.3%)	1 (16.7%)
($n = 15$)	Delayed 2	12 (75.0%)	3 (25.0%)	0	8 (53.3%)	7 (46.7%)	0
Malignant	Early	4 (36.3%)	2 (18.2%)	5 (45.5%)	3 (27.2%)	4 (36.4%)	4 (36.4%)
lesions ($n = 11$)	Delayed 1	2 (18.2%)	3 (50.0%)	6 (33.0%)	2 (18.3%)	6 (54.5%)	3 (27.2%)
	Delayed 2	5 (45.5%)	6 (54.5%)	0	3 (27.2%)	8 (72.8%)	0



a b c d

Figure 1 Axial CT scan of a typical parotid pleomorphic adenoma, obtained (a) initially and then (b) 30 s, (c) 120 s and (d) 8 min after intravenous administration of contrast material. Note progressive increment of degree and homogeneity of the enhancement; it becomes strong and homogeneous in (d) the second late phase

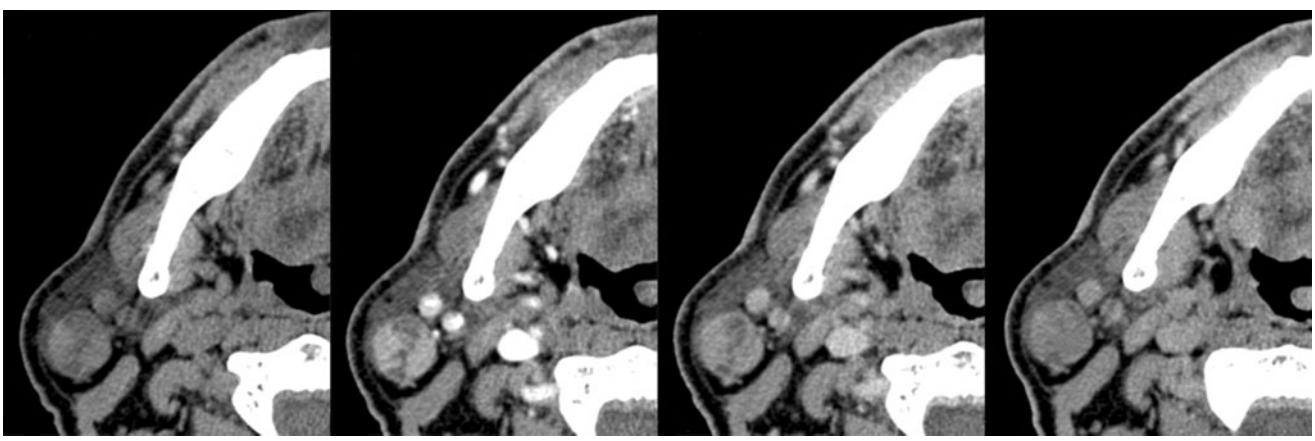


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Figure 2 Axial CT scan of a typical parotid pleomorphic tumour, obtained (a) initially and then (b) 30 s, (c) 120 s and (d) 8 min after intravenous administration of contrast material. Another case of parotid pleomorphic adenoma with characteristic delayed enhancement

Table 2 The best homogeneity pattern of the enhancement of pleomorphic adenoma in each phase: a statistical evaluation in the differential diagnosis between pleomorphic adenoma and non-pleomorphic adenomas

Time after contrast injection	*Most sensitive homogeneity of enhancement pattern of pleomorphic adenoma*	*Specificity (%)*	*PPV (%)*	*NPV (%)*
30 s	Not homogeneous 77.7% (28/36)	68.75	84.85	57.89
120 s	Not homogeneous 52.77% (19/36)	50.00	70.37	32.00
8 min	Uniform 100% (36/36)	100	100	100

PPV, positive predictive value; NPV, negative predictive value

Table 3 The most sensitive degree pattern of the enhancement of pleomorphic adenoma in each phase: a statistical evaluation in the differential diagnosis between pleomorphic adenomas and non-pleomorphic adenomas

Time after contrast injection	*Most sensitive degree of enhancement pattern of pleomorphic adenoma*	*Specificity (%)*	*PPV (%)*	*NPV (%)*
30 s	Low 69.44% (25/36)	75.00	86.20	52.17
120 s	Moderate 58.33% (21/36)	56.25	70.00	31.81
8 min	Strong 61.11% (22/36)	100	100	53.33

PPV, positive predictive value; NPV, negative predictive value

sensitivity, specificity, PPV and NPV of 100%; see Table 3).

Discussion

Pleomorphic adenoma is the most common tumour of the salivary glands;[8] generally, it is a benign and slow-growing tumour. It is more frequent in women than in men and has a peak incidence at 40 years.[8] From the anatomopathological point of view, the pleomorphic adenoma shows a variegated pattern due to the presence of areas with epithelial differentiation (solid adenoid areas) and areas with mesenchymal-like differentiation (chondroid myxoid areas).[9]

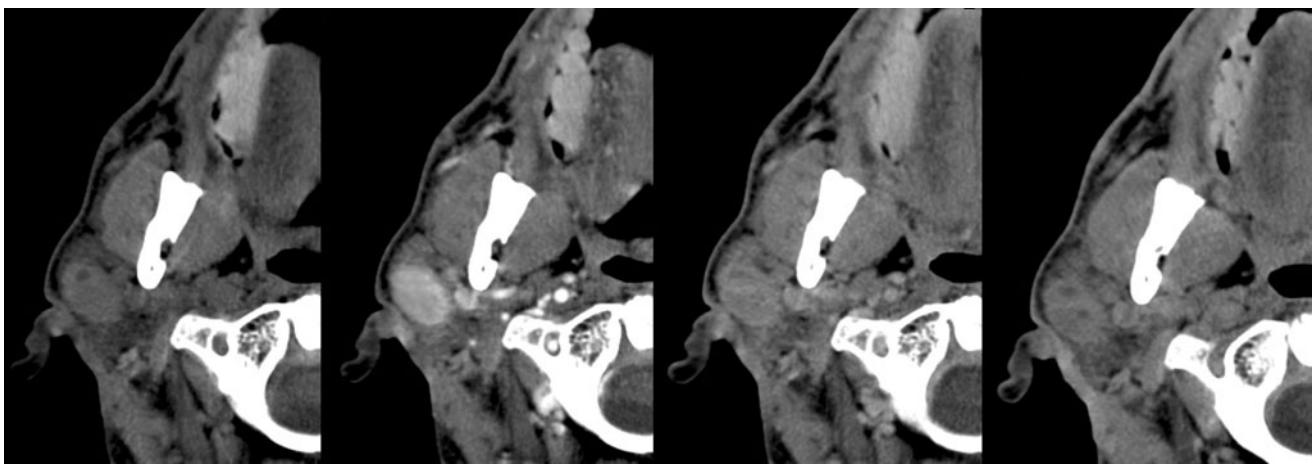
It is often surrounded by a capsule (not always intact) and sometimes it has satellite micronodules.[10]

Due to the presence of multifocal lesions, total parotidectomy with preservation of the facial nerve is the most common therapy to avoid post-surgical recurrences.[1] In the long term, a malignant degeneration may occur; this is more likely in adenomas older than 10 years. Therefore, early diagnosis is necessary and should be followed by the appropriate therapeutic approach.[6]

The literature includes studies that characterize parotid lesions on the basis of their behaviour after contrast administration, through study protocols developed on two dynamic phases (30 s and 120 s scan delay).[11]

Results were not completely satisfying; they showed that during the 120 s delayed phase, adenomas showed a modest enhancement increase; Warthin's tumours showed a decrease and malignant tumours showed an increase or no change at all.

Other authors have recently used more delayed phases to better study parotid lesions: the pathognomonic behaviour of the pleomorphic adenoma enhancement was already clear, becoming stronger and more homogeneous in delayed phases.[12,13]



a b c d

Figure 3 Axial CT scan of a typical parotid Warthin's tumour, obtained (a) initially and then (b) 30s, (c) 120s and (d) 8 min after intravenous administration of contrast material. Enhancement is strong and homogeneous in (b) the first post-contrast phase; it becomes weak/moderately homogeneous in (d) the second late phase

Our study aimed at investigating the interesting hints from the literature and at enrolling more patients to confirm the usefulness of this three-phase study, followed by a delayed phase for the assessment of parotid lesions.

On the basis of our experience, triphasic CT of parotid tumours was more useful than biphasic examination for characterizing lesions. The first technique, indeed, provides a better differentiation of the anatomopathological characteristics between pleomorphic adenomas and non-pleomorphic adenomas.

In particular, the hypovascularization of pleomorphic adenomas was better assessed; it is responsible for the delay by which the enhancement of the lesions becomes strong and homogeneous.

Data from the early phase proved to be reliable only in ruling out the pleomorphic adenoma in cases in which the enhancement of the lesion was strong and uniformly homogeneous.

In all other cases, the diagnosis was doubtful; it was not even possible to differentiate between benign and malignant lesions.

The analysis of the lesions' enhancement patterns in the first delayed phase allowed us to rule out the diagnosis of pleomorphic adenoma when the degree and homogeneity of the enhancement were reducing. However, it was not possible to discriminate with high specificity the pleomorphic adenoma from malignant tumours in cases where the degree and homogeneity of the enhancement either increased or remained unchanged.

Thus, the second delayed phase proved to be extremely useful; it clearly showed the difference between pleomorphic adenomas and malignant tumours.

In adenomas, enhancement was always stronger and more homogeneous while malignant tumours (more vascularized) showed an opposite trend.

Table 2 shows the statistical value of the most frequent degree and homogeneity patterns of the enhancement of pleomorphic adenoma in each phase, to identify the most effective phase for the differential diagnosis between pleomorphic adenoma and other adenomas.

Results clearly show that the 8 min after contrast administration phase is the most effective phase for the differential diagnosis between pleomorphic adenoma and non-pleomorphic adenomas; strong enhancement and uniform enhancement, indeed, showed specificity, PPV and NPV values higher than the most sensitive patterns of pleomorphic adenoma obtained in the other two post-contrast phases.

In particular, the best accuracy pattern was uniform enhancement because (according to its PPV and NPV of 100%) its presence/absence allowed a certain differential diagnosis.

This result entails important implications not only for the radiological evaluation of the lesions (*i.e.* examining CT scans knowing it is a benign lesion), but also for the diagnosis, to avoid unnecessary biopsies and to clear up potential doubts from the biopsy in the event of sampling mistakes or atypical histological variances.

This technical protocol can be particularly useful in the case of lesions located in the deep extension of the parotid gland; these lesions could not be assessed by ultrasound and, due to their location, the biopsy was not easy to perform.[14]

As previously said, the results from the three radiologists were the same in all three phases both for the degree and homogeneity of the enhancement, proving that the study can be easily reproduced.

The subjective assessment of the degree and homogeneity of the enhancement in the different phases was confirmed by the empirical assessment of the CT number of lesions by drawing a region of interest.

The confirmation of correspondence of the degree (low, moderate, strong) and of the homogeneity of enhancement (low, moderate, uniform) to numerical values provides the subjective analysis of CT examinations with objective data confirming the radiologist's personal opinion.

On the basis of our results, obtained on the broadest population reported in literature regarding CT parotid studies, we think that our technique might represent the basis for the improvement of this technical protocol to be regularly applied in CT examinations of parotid enlargements.

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