

Diagnostic work-up of parotid neoplasms

WHO Histological Classification 2005

Malignant epithelial tumours			
Acinic cell carcinoma	8550/3	Basal cell adenoma	8147/0
Mucoepidermoid carcinoma	8430/3	Warthin tumour	8561/0
Adenoid cystic carcinoma	8200/3	Oncocytoma	8290/0
Polymorphous low-grade adenocarcinoma	8525/3	Canalicular adenoma	8149/0
Epithelial-myoepithelial carcinoma	8562/3	Sebaceous adenoma	8410/0
Clear cell carcinoma, not otherwise specified	8310/3	Lymphadenoma	
Basal cell adenocarcinoma	8147/3	Sebaceous	8410/0
Sebaceous carcinoma	8410/3	Non-sebaceous	8410/0
Sebaceous lymphadenocarcinoma	8410/3	Ductal papillomas	
Cystadenocarcinoma	8440/3	Inverted ductal papilloma	8503/0
Low-grade cribriform cystadenocarcinoma		Intraductal papilloma	8503/0
Mucinous adenocarcinoma	8480/3	Sialadenoma papilliferum	8406/0
Oncocytic carcinoma	8290/3	Cystadenoma	8440/0
Salivary duct carcinoma	8500/3		
Adenocarcinoma, not otherwise specified	8140/3	Soft tissue tumours	
Myoepithelial carcinoma	8982/3	Haemangioma	9120/0
Carcinoma ex pleomorphic adenoma	8941/3		
Carcinosarcoma	8980/3	Haematolymphoid tumours	
Metastasizing pleomorphic adenoma	8940/1	Hodgkin lymphoma	
Squamous cell carcinoma	8070/3	Diffuse large B-cell lymphoma	9680/3
Small cell carcinoma	8041/3	Extranodal marginal zone B-cell lymphoma	9699/3
Large cell carcinoma	8012/3		
Lymphoepithelial carcinoma	8082/3	Secondary tumours	
Sialoblastoma	8974/1		
Benign epithelial tumours			
Pleomorphic adenoma	8940/0		
Myoepithelioma	8982/0		

¹ Morphology code of the International Classification of Diseases for Oncology (ICD-O) (821) and the Systematized Nomenclature of Medicine (<http://snomed.org>) Behaviour is coded /0 for benign tumours, /3 for malignant tumours, and /1 for borderline or uncertain behaviour.

Frequency of different histotypes

		n	Muco epidermoid ca	Adenoca NOS	Adenoid Cystic ca	Acinic ca	Ca ex Pl. ad
Spiro	1989	256	51 %	11 %	6 %	8 %	18 %
Frankenthaler	1991	155	35 %	10 %	11 %	11 %	5 %
Rehman	1996	190	16 %	18 %	23 %	11 %	11 %
Magnano	1999	97	16 %	13 %	14 %	7 %	9 %
Godballe	2003	75	12 %	13 %	17 %	27 %	15 %
Teerhard	2004	332	16 %	26 %	15 %	17 %	9 %
Zbären	2009	183	18 %	8 %	8 %	16 %	12 %
Overall		1'287	27 %	17 %	14 %	13 %	11 %

Topics

► Imaging studies

Fine needle aspiration cytology

Value of FNAC for Pleomorphic Adenoma

Frozen section analysis

Immunohistochemical typing comparison between FNAC and FS

Indications

Extent of the mass is uncertain

Massive or fixed tumor

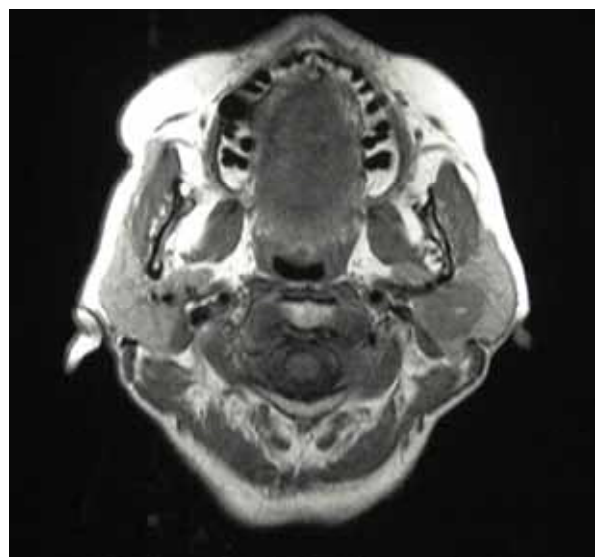
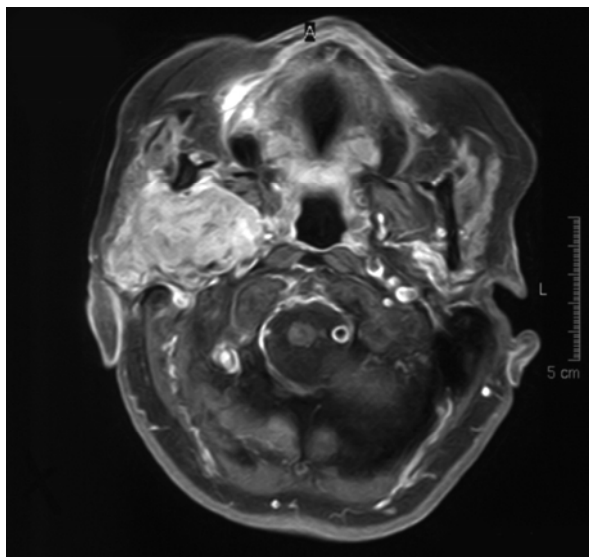
Tumor extends into or involves the parapharyngeal space

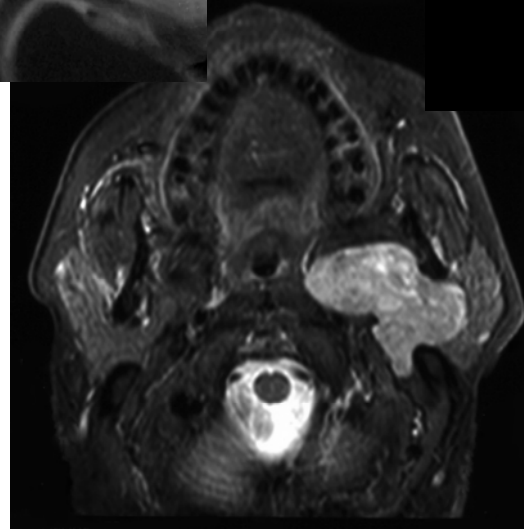
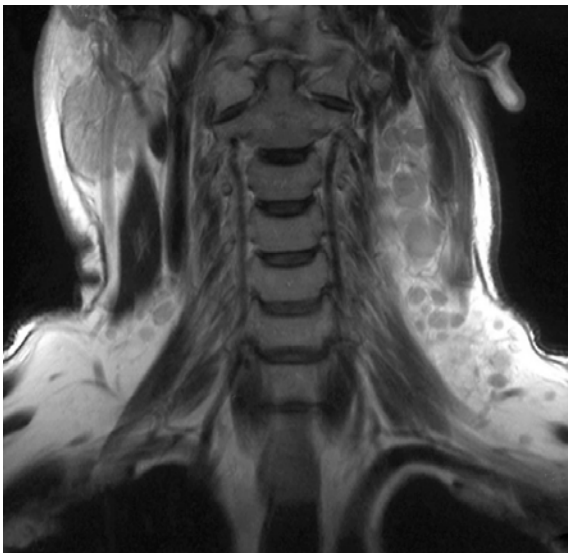
Recurrent tumor

Clinical suspicion of malignancy

O'Brien et al Head Neck 2003

- ▶ **Relation between tumor and surrounding tissue**
- ▶ **Localization of the tumor**





Topics

► Imaging studies

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Value of FNAC for Pleomorphic Adenoma

Frozen section analysis

Typing comparison between FNAC and FS

Arguments against FNAC

- ▶ Relative value of FNAC in distinguishing among the various types of malignancies
- ▶ Minor influence of FNAC on treatment planning
- ▶ „FNAC seldom adds to the work-up of patients with a parotid mass but contributes to the patient's expense...“

Olsen Postgrad Med 1987
Hee Aust NZ J Surg 2001
Fee Arch Otolaryngol Head Neck Surg 2003

Advantages of FNAC

Preoperative information about the malignant nature can be helpful in

- ▶ Preventing treatment delay
- ▶ Informing the patient on the treatment plan and the possible risk of facial nerve injury
- ▶ Achieving wide tumor-free excision margins
- ▶ Assessing and establishing a policy toward neck lymph nodes

Aim of the Study

To compare the results of FNAC with the histopathologic diagnosis

To evaluate the accuracy, sensitivity, specificity in identifying parotid malignancies

To evaluate the accuracy, sensitivity, specificity in identifying pleomorphic adenomas

To analyze the false positive and false negative findings

Patients

n = 435

Malignant Tumors **178 (41%)**

Primary parotid carcinoma **137**

Lymphoma **14**

Secondary tumor **27**

Benign Tumors **257 (59%)**

Pleomorphic adenoma **161**

Warthin tumor **64**

Monomorphic adenoma **15**

Inflammatory lesions and cysts **17**

Classification

Nondiagnostic	A cytologic diagnosis could not be made on the basis of the material obtained
True negative	Absence of malignancy was correctly diagnosed
True positive	Presence of malignancy was correctly diagnosed (includes specimens interpreted as suspicious for malignancy)
False negative	The cytologic specimens failed to diagnose a malignancy
False positive	The cytologic specimen was incorrectly considered for malignancy

Institutional Experience

n = 435

Nondiagnostic smears		17	(4%)
True - positive	for malignancy	126	(29%)
True - negative	for malignancy	239	(55%)
False - positive	for malignancy	8	(2%)
False - negative	for malignancy	45	(10%)

Results

Diagnosis of malignant lesions

Accuracy	87%
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Specificity	97%
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Sensitivity	74%
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Pos. pred. value	94%
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Neg. pred. value	84%
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Results

True positive findings **n = 126**

Primary parotid ca	98/130	(75%)
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Secondary tumors	25/27	(93%)
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Lymphoma	3/13	(23%)
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Results

True negative findings n = 239

Pleomorphic adenoma 152/156 (97%)

Warthin tumor 59/61 (97%)

Monomorphic adenoma 11/14 (79%)

Inflammatory lesions and cysts 17/17 (100%)

Results

False negative findings n = 45 (10%)

Histology		Cytology	
8/15 (53%)	Ca ex pl. adenoma	7	Pl. adenoma
		1	Normal salivary gland tissue
6/12 (50%)	Adenoid cystic ca	4	Pl. adenoma
		1	Hemorrhagic cyst
		1	Epithelial myepithel tumor
10/13 (77%)	Lymphoma	7	Unspec. lymphadenitis
		3	Lymph node
6/25 (24%)	Acinic cell ca	4	Monom. adenoma
		1	Warthin tumor
		1	Sialadenitis
6/24 (25%)	Mucoepidermoid ca	2	Warthin tumor
		1	Pl. adenoma
		1	Lymphoepithelial lesion
		1	Intraduct. papilloma
		1	Cystic lesion

Results

False negative findings n = 45 (10%)

Histology		Cytology	
2/15	Salivary duct ca	1	Pl. adenoma
		1	Cystic lesion
2/5	Myoepithelial ca	2	Pl. adenoma
1/12	Adenoca NOS	1	Papillary adenoma
1/1	Terminal duct ca	1	Parotid tissue
1/3	Undiff. ca	1	Unspecific Lymphadenitis
2/27	Metastases	1	Cystic Lesion
		1	Pl. adenoma

Results

False positive findings n = 8 (2%)

Histology		Cytology	
4/156 (2.5%)	Pl. adenoma	1	Mucoepidermoid ca
		1	Ca ex pl. adenoma
		1	Adenoid cyst ca
		1	Carcinoma NOS
3/14 (21%)	Monomorphic adenoma	2	Mucoepidermoid ca
		1	Adenoid cystic ca
1/61 (1.6%)	Warthin tumor	1	Mucoepidermoid ca

Discussion

The relatively high rate of false-negative findings is a problem that has been debated in many studies and has been reported to range from 14 - 48%

Chan MKM	Acta Cytol	1992; 36: 353 - 363
Zurrada S	Cancer	1993; 72: 2306 - 2311
Atula T	Diagn Cytopathol	1996; 15: 185 - 190
Al-Khafaji BM	Cancer	1998; 84: 153 - 159
Costas A	Br. J Oral Maxillofac Surg	2000; 38: 539 - 542
Stewart CJR	Diagn Cythopathol	2000; 22: 139 - 146
Que He CG	Aust N Z J Surg	2001; 71: 345 - 348
Lurie M	Isr Med Assoc J	2002; 4: 681 - 683

Discussion

In acinic cell carcinomas and low grade mucoepidermoid ca., **classic morphologic parameters**, such as necrosis, mitotic figures and nuclear atypia, are **rare** or **absent**, giving rise to a relatively high rate of false negative findings

Discussion

The most commonly misdiagnosed salivary gland lesions on FNAC

	Histology	Cytology
False negative	Lymphoma	Benign lymph node
	Acinic cell ca	Normal parotid tissue
	Mucoepid ca low grade	Benign cyst
	Ca ex pl ad	PI adenoma
	SCC	Sialadenitis
False positive	Monom. adenoma	ACC
	Intraparotid. lymph node	Lymphoma
	Warthin tumor	

Alphs HHCurr Opin Otolaryngol Head Neck Surg 2006; 14: 62 - 66

Discussion

Klijanienko J Diagn Cytopathol 1999; 21:163-166

Ca ex pl. adenoma **26**

False negative findings **11 (42%)**

Discussion

Zurrida S et al Cancer 1993;72:2306-11

Lymphoma	7
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False negative findings	5 (71%)
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Discussion

Klijanienko J Diagn Cytopathol 1997; 17:92-98

Low grade mucoepidermoid ca	22
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False negative findings	7 (32%)
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Discussion

Many false-negative findings are due to sampling errors rather than on misinterpretation of cytologic smears; this is especially valid for

- ▶ Ca ex plemorphic adenoma
- ▶ Lymphoma

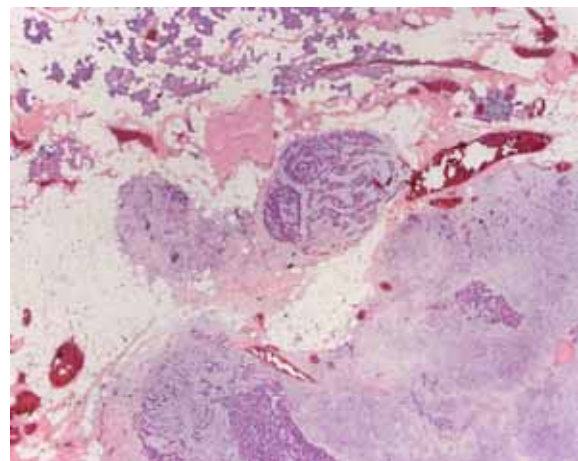
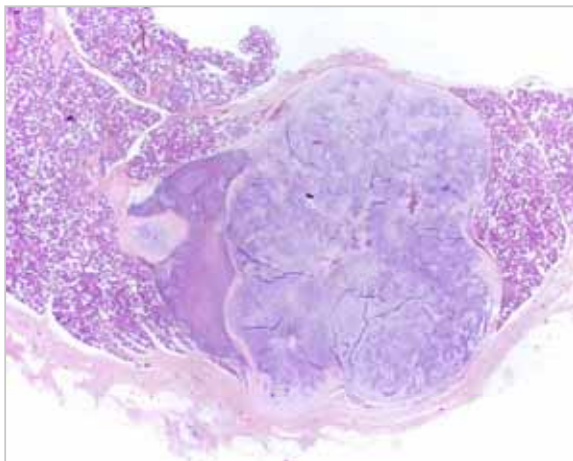
Discussion

Problems comparing FNAC results

- ▶ Nonneoplastic lesions included versus excluded
- ▶ Recurrent tumors included versus excluded
- ▶ FNAC performed by clinicians versus cytopathologists

Literature

		n	Sensitivity	Specificity	Accuracy
Atula	1996	218	55%	92%	
Al-Khafaji	1998	154	82%	86%	84%
Schröder	1998	336	93%	99%	98%
Steward	2000	341	92%	100%	98%
Postema	2004	280	88%	99%	96%
Seethala	2005	220	86%	92%	90%
Presented study	2009	435	74%	97%	87%



Value of FNAC for Pleomorphic Adenoma

Institutional Experience

n = 435

Benign lesions	257
Pleomorphic adenoma	161
Malignant tumors	178
Nondiagnostic	17 (4%)
True - positive for PA	144 (33%)
True - negative for PA	247 (57%)
False - positive for PA	14 (3%)
False - negative for PA	13 (3%)

Pleomorphic Adenoma

Findings in detecting PA

Accuracy	93%
Sensitivity	92%
Specificity	94%
Pos. pred. value	91%
Neg. pred. value	95%

False positive for Pleomorphic Adenoma

n = 14 (3%)

Ca in pleomorphic adenoma	7
Adenoid cyst ca	4
Myoepithel ca	2
Salivary duct ca	1

False negative for Pleomorphic Adenoma

n = 13 (3%)

Mucoepidermoid carcinoma	1
Ca ex pleomorphic adenoma	1
Carcinoma	1
Epithelial / myoepithelial tumor	3
Cystic lesion	2
Lipoma	1
Neuroma	1
Warthin tumor	1
Benign lesions	2

Topics

► Imaging studies

Fine needle aspiration cytology

Use of FNAC for Pleomorphic Adenoma

Frozen section analysis

Tumor typing comparison between FNAC and FS

Indications

- **Discordance between FNAC findings and clinical / radiological findings**
- **Instances in which FS is going to offer information that could alter treatment**
- **Cytology and / or clinical findings are suggestive of malignancy**

Institutional Experience: Patients

n =156

Malignant Tumors

94

Primary parotid carcinoma

78

Lymphoma

8

Secondary tumor

6

Radiation induced carcinoma

2

Benign Tumors

62

Pleomorphic adenoma

39

Warthin tumor

11

Monomorphic adenoma

8

Inflammatory lesions and cysts

4

Results

Parotid neoplasms

156

Nondiagnostic specimens

2

True - positive

89

True - negative

57

False - positive

2

False - negative

6

Results

Diagnosis of malignancy of parotid tumors by frozen section

Sensitivity	94%
Specificity	97%
Accuracy	95%
Positive predictive value	98%
Negative predictive value	90%

Results

False positive findings **n = 2**

Histology

Frozen section

2 pleomorphic adenomas

1 Epithel. myoepith. ca

1 Suspicious for malignancy

Impossible to determine **n = 2**

Monomorphic adenoma

Acinic cell carcinoma

Results

False negative findings **n = 6**

Frozen section	Histology
Sarcoidosis Pl. adenoma Ductal papilloma	3 Mucoepidermoid ca
Pl. adenoma	1 Ca ex pleomorphic adenoma
Oncocytoma	1 Myoepithelial carcinoma
Plemorphic adenoma	Adenocystic carcinoma

Results

The exact **histologic** tumor **type** was

not mentioned		15
mentioned		131
correct	120	(92%)
incorrect	11	(7%)
Malignat tumors	65/75	(87%)
Benign tumors	55/56	(98%)

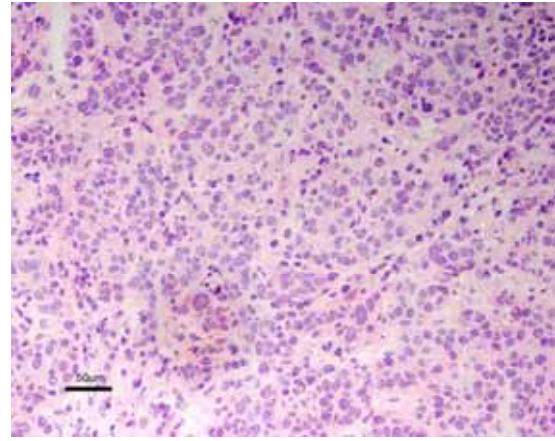
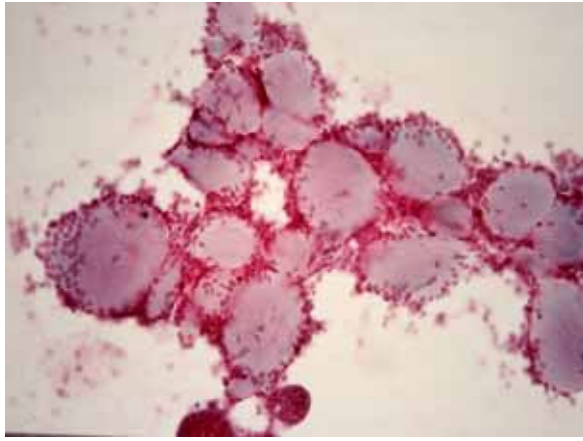
Literature

		n	Sensitivity	Specificity	Accuracy
Megerian	1994	170	91	98	97
Zheng	1997	65	87	98	95
Tew	1997	159	96	99	95
Seethala	2005	57	77	100	88
Present study	2007	153	94	97	95

Summary

The superiority of FS over FNAC was demonstrated

Most false negative and all false positive FNAC findings were correctly evaluated by FS



Tumor typing

Comparison between FNAC and FS

FNAC and FS

n = 110

Malignant tumors	68
Primary parotid ca	60
Lymphoma	8
Benign tumors	42
Pleomorphic adenoma	26
Warthin tumor	6
Monomorphic adenoma	6
Inflammatory lesions	4

FNAC and FS in detecting malignancy

	FNAC	FS
Sensitivity	74%	93%
Specificity	88%	95%
Accuracy	79%	94%
PPV	91%	97%
NPV	67%	89%

FNAC and FS in detecting malignancy

FNAC		FS		
		Correct	False	Not mentioned
FNAC true pos	50	47	3	
FNAC true neg	37	35	1	1
FNAC false pos	5	5		
FNAC false neg	18	17	1	

Tumor typing by FNAC

True positive for malignancy 50

True negative for malignancy 37

	malignant neoplasms	benign neoplasms
correct	24 (48%)	27 (74%)
false	12 (24%)	5 (13%)
not mentioned	14 (28%)	5 (13%)

Tumor typing by FS

True positive for malignancy 63

True negative for malignancy 40

	malignant neoplasms	benign neoplasms
correct	49 (78%)	39 (97%)
false	4 (6%)	1 (3%)
not mentioned	10 (16%)	

Tumor typing

n=110

	FNAC	FS
correct	59%	85%
false	19%	5%
not mentioned	22%	10%

Summary

- ▶ FNAC is prone to **avoid** surgery or to **limit surgical procedures** for benign neoplasms
- ▶ FNAC is **not qualified to plan the extent of surgical procedures** in primary parotid carcinomas
- ▶ **Only FS is prone to expand the surgical procedure** (superficial → total parotidectomy; neck dissection)

Summary

Tumor typing by FNAC (n=110)

The accuracy for benign tumors was significantly higher than for malignant tumors

61% versus 33% ($p < 0,05$)

Tumor typing by FS (n=110)

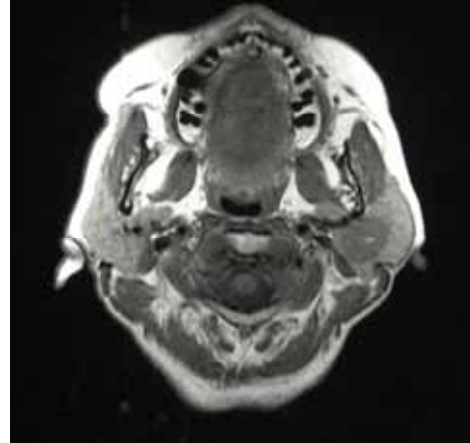
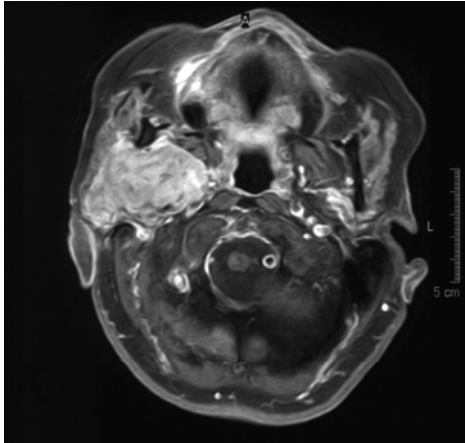
93% of benign tumors **versus 72%** of malignant tumors were typed accurately



Thank you

Imaging Studies

- ▶ Relation between tumor and surrounding tissue
- ▶ Localization of the tumor
- ▶ Multinodularity
- ▶ Lymph node metastases



Neoplasms of the Parotid Gland

Frozen section analysis

Indications

- ▶ Discordance between FNAC findings and clinical / radiological findings
- ▶ Instances in which FS is going to offer information that could alter treatment
- ▶ Cytology and / or clinical findings are suggestive of malignancy

Frozen Section

Parotid neoplasms 153

		FNP
Accuracy	94%	88%
Sensitivity	91%	75%
Specificity	96%	95%

