# Pleomorphic Adenoma Review of Surgical Management with a focus on histopathological aspects

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## Abstract

Salivary Gland Tumors arise in the Parotid gland in about 80% of cases[2, 3]. Benign parotid gland tumors account for 80% of cases [3]. Around 80 percent of all benign salivary glands' tumors are pleomorphic adenomas, which are the most frequent salivary gland tumor overall (between 50 and 70 percent) [2-4]. Despite their benign nature, Pleomorphic Adenomas can occasionally result in benign metastases and carry the potential to evolve into malignancy [1, 5–9]. The main course of treatment is surgical excision, where the optimal extent of surgery has been an area for debate. The Pleomorphic adenoma is known for hard-to-treat multilocular recurrences, hence it is widely advocated to remove the whole or at least the superficial part of the gland with the tumor as a standard treatment to avoid recurrences based on the evidence of histological presence of pseudopods and satellite nodule but other advocate minimal intervention removing only the tumor with cuff of normal tissue around it and presenting evidence of comparable recurrence rates to traditional approach and lower complications rate compared to it. They argue that the cuff of normal tissue will include satellite nodule and pseudopod based on histological measurements.

Keywords: Salivary Gland, Parotid, Parotid Gland, Pleomorphic Adenoma, Mixed Tumor, Complete Parotidectomy, Partial Parotidectomy, Superficial Parotidectomy, Lateral Parotidectomy, Extracapsular Dissection,

## Introduction

Salivary gland tumors account for 6% of all head and neck tumors[1]. In about 80% of the cases, tumors arise in the Parotid gland[2, 3]. 80% of parotid gland tumors are benign [3]. Pleomorphic adenoma is the most common Salivary gland tumor overall (50-70 %) and accounts for about 80% of all benign tumors [2-4]. Though benign in nature, Pleomorphic Adenoma can in rare cases give benign metastasis and they harbor malignancy transformation [1, 5-9]. The primary treatment is surgical removal, but this can be extremely challenging in some cases because of unusual localization or extensive growth. [10-13].

## Histopathology

Pleomorphic Adenoma is the most common Salivary gland tumor with an annual incidence of 3.5/100,000. Histologically the tumor is in 96% of the cases under 4 cm and is composed of epithelial and stromal components. Genetic events leading to the development of Salivary Glands Pleomorphic Adenomas are alterations involving Pleomorphic Adenoma Gene 1 (8q12) (PLAG1) encoding for cell cycle progression zinc finger protein, HMGA2 gene (12q13-15) encoding High-mobility group protein and sporadic, clonal changes [1, 15, 16]. Depending on the Stromal component of the tumor Pleomorphic Adenoma can be either Myxoid (Stroma rich with >80% Stromal component), Cellular ( 20-30% Stromal component), or Classical (Balanced with 30-50% Stromal component)[17]. In about 50 %, the tumor is Stroma rich variant where the Cellular variant makes up 35% of the cases, and the remaining 15% are Classical [4, 18]. Stroma has a spectrum of components ranging from Myxoid, Chondroid (the former two are present in >80% and usually with abundance), Lipomatous, and Osseous (only in 2% of the cases and up to only 5% of the stroma). Histologically there is a usual abundance of plasmacytoid and spindle cells whereas other cell types, oval, epithelioid, and clear, are less common and can be seen in an island form, where finding of Ductal atypia, diffuse fibrosis, and necrosis raise the suspicion level of malignant transformation [1, 4]. The tumor has a capsule ranging from 5-250 micrometers. Stennert et al. studied 100 cases of pleomorphic adenoma, where focal capsule absence was seen in 43% of the cases making up to 4% of the entire tumor capsule for all tumor variants. This finding was more prominent in myxoid tumors and involved 28% of the entire circumference. He defined an area with a thickness <20 micrometers as a thin capsule; with this definition, all tumors had a focally thin capsule for up to 20% of the entire tumor circumference[18]. Another aspect of the capsule is tumor ingrowth that is continuous with the main tumor in the fibrous; this finding is designated with different terms in the literature such as capsular herniation/penetration, tumor buds, or nodular protrusion, and this is present in 28% of the cases. Pseudopodia is defined as an island of tumor separated from the main tumor but still within the capsule whereas satellite nodules are separated from both the capsule and the main tumor. Pseudopodia was found in 40% of the cases while satellite nodules in only 13%[16].

## Imaging

The hallmark of pleomorphic adenoma in ultrasound examination is a lobulated, well-defined contour; the tumor is usually homogenous with low vascularity. On Sonoelastography, it demonstrates the so-called “dense core” sign[19, 20]. MRI is the second choice, especially in difficult-to-assess deep tumors or extensive growth. In MRI, the tumor exhibits low to intermediate intensity on T1, and the cellular part will correspond to a high-intensity area, whereas the myxoid will give a higher intensity[21]. CT is rarely needed, but it can be useful in showing bony involvement. A well-defined sometimes lobulated mass with either heterogeneous or homogeneous contrast enhancement can be demonstrated[22].

## Recurrence

At one historical point of time , recurrence rates were extremely high 25%-88.9%. This dropped down drastically after the abandonment of Enucleation which left the tumor capsule behind[23, 24]. A high-risk factor for recurrence includes young age at first diagnosis. Patients who have recurrences tend to be about ten years younger than those who do not [1, 14, 25]. Margin Status, Tumor Spillage is associated with 80% while capsule puncture has a 26.9% risk of recurrence. Uncertain margin status from the initial therapy also accounts for a risk factor[1, 14].

Recurrences are in most cases (90%) multinodular with a mean number of nodules 26-58 and nodule numbers ranging from 2-266[14, 26]. Multilocularity is a risk factor for the second recurrence. Pathological examination has revealed more nodules when compared to MRI findings. Nodules were constantly found in the first tumor resection bed, but in 80%, there were nodules observed outside the scar, impeded in healthy surrounding fat tissue or other parts of the gland[26].

In a nationwide study In the Netherlands, recurrences had a median interval of 7 years; there was a recurrence risk of 6.4% with a 1.1% risk of recurrence between 15-20 years after the first tumor. Second recurrences (16%) were encountered mainly in the first five years after the first recurrence. The risk of malignant transformation was 3.2% for all recurrence patients[14]. Another study showed thatrecurrence occurred from 1 to 16 years, but only 12% were diagnosed through regular follow-up [27]. In our Institute, we conduct a yearly ultrasound follow-up. MRI is rarely needed, and we believe that patients are more compliant with a quick ultrasound examination done by our ENT residents. The role of adjuvant radiotherapy is not well standardized; in one study group there were 34 patients with a different number of recurrences and multinodular disease and positive microscopic margins, but none had a gross residual of tumor, received 45-60 Gy Radiation therapy dose as adjuvant therapy. 94% local control was achieved; one patient developed mucoepidermoid carcinoma 14 years after therapy[28].

## Current Opinion on Surgical Intervention

After the abandonment of Enucleation because of high recurrence rates, Total Parotidectomy (total resection of both superficial and deep lobe with preservation of facial nerve) was adopted as a surgical option. Many surgeons went for an even lesser variant like Superficial/ Lateral Parotidectomy (resection of the superficial lobe lateral to the facial nerve with nerve dissection) or a Partial superficial parotidectomy (resection of part of the lateral lobe with facial nerve main trunk preparation) or an Extracapsular Dissection (Tumor with a cuff of normal tissue without main trunk preparation)[29]. There is debate about if lesser variant especially Extracapsular Dissection pays enough respect to tumor histological features especially satellite nodule and pseudopodia[18]. On the other side, many studies show that EC, PSP, SP, and TP all have similar recurrence rates. The argument for extracapsular dissection is shorter operation time, less complication rate especially Frey syndrome, and better cosmetic satisfaction, as well as an easier revision if needed as the facial nerve is not in the resection bed [23, 29, 30]. It needs to be said that accumulation of experience as demonstrated in the institutional learning curve in a Reference center in Germany as reported by Mantsopoulos et al.[31] helps to refine and optimize surgical outcome and procedure for extracapsular dissection, which leaves lateral parotidectomy as a choice for a more standardized approach for centers that deal with a low number of cases.

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