Ameloblastoma is unicentric, non-functional, intermittent in growth, anatomically benign and clinically persistent tumor of the oral and maxillofacial region. Ameloblastoma is the second most common odontogenic tumor in the oral and maxillofacial region. It represents about 1% of all oral odontogenic epithelial tumors and 11% of all odontogenic tumors. Three groups namely multicystic, unicystic and peripheral are recognized in the clinico-radiological classification. Various non-invasive radiographic analytic methods determine the diagnosis and prognosis of ameloblastoma. Targeted therapy against various genes is a promising therapeutic modality for Ameloblastoma. Hence future research can be directed towards non-invasive or minimally invasive diagnostic techniques and targeted therapies.

**Keywords:** Ameloblastoma • Cone-beam computed tomography • Radiography • Targeted therapy

**Description**

Ameloblastoma is an aggressive odontogenic tumor mainly in the oral and maxillofacial region formed from odontogenic epithelium within a fibrous stroma devoid of odontogenic ectomesenchyme [1]. The global incidence of ameloblastoma is around 0.5 cases per million per year with the site predilection of posterior mandibular region [2]. Six histopathologic variants of ameloblastoma are recognized: follicular, plexiform, acanthomatous, basal cell, granular cell, and desmoplastic [3]. The follicular and plexiform patterns are more common. Mandibular lesion accounts nearly 80% of the ameloblastoma and occurrence in maxilla is rare [4]. Three clinico-radiologic groups namely solid or multicystic, unicystic and peripheral are recognized. The radiological diagnosis of ameloblastoma includes intraoral radiography, extra oral radiography (orthopantomogram and cephalogram), Cone Beam Computed Tomography (CBCT), Computed Tomography(CT), Magnetic Resonance Imaging(MRI) etc. [5].

Cone Beam Computed Tomography imaging is an emerging diagnostic modality in oral and maxillofacial region for ameloblastoma. It reveals the three dimensional morphology/anatomy, precise internal structure, spatial relation, geometric relation to anatomical structure, cortical expansion, trabecular bone changes, peripheral extensions, density of bone and measurements [3]. The three dimensional model and the spatial relationship can aid in treatment planning. CBCT has higher isotropic spatial resolution and lower radiation dosage compared to Multi-Detector Computed Tomography (MDCT) [5]. It depicts sub-millimeter structures and the clustering of calcifications internally and in adjacent areas [6]. The internal structure and adjacent trabecular changes can aid in elimination of differential diagnosis. Thinning of cortical plate, perforation in cortical bone and thickness of the cortical bone in sagittal, coronal and axial section can be evaluated by CBCT which determines the prognosis of the disease [7].

Spatial relationship of the lesion with mandibular canal and mental foramen/mandibular foramen can be established by nerve tracing and mirrored-method analysis [8]. Root resorption, pattern of resorption, tooth displacement in three dimension and lamina dura morphology can be computed through CBCT [9]. The maxillary ameloblastoma can have its effect on the maxillary sinus, nasal cavity and orbital floor. The expansion of ameloblastoma into the sinus or orbits can be precisely diagnosed using CBCT including the measurement of dimension and the intactness of the walls/orbit. The nasopatellar nerve canal involvement especially in the maxillary anterior ameloblastoma can be established through CBCT. The diagnosis of ameloblastoma using CBCT showed greater sensitivity (77.33%) and specificity (90.00%) comparing the orthopantomogram (61.33% and 86.00%) [10]. The current techniques such as segmentation analysis, fractal analysis, deep learning techniques, texture analysis, pattern analysis, fusion imaging in CBCT can explore various arenas in diagnostic analysis through further research alongside 4 dimensional imaging and artificial intelligence. The fractal analysis and texture analysis can determine the trabecular pattern of bone by analyzing the trabecular bone and bone marrow detecting the early changes in alveolar bone including the peripheries. The fusion imaging can detect and assess the prognosis of the disease by comparing the preoperative and postoperative images.

The main treatment modalities for ameloblastoma treatment include conservative surgical enucleation, radical surgery, bone curettage, electrocautery, radiation therapy or combination of radiation and surgery. Though surgical excision is the commonest modality of treatment, various modern non-invasive alternatives are surfacing through genetic engineering. Vemurafenib, a BRAF (proto-oncogene B-Raf) inhibitor, is newer therapeutic modality recommended in local aggressive ameloblastoma lesions and as alternative to surgical treatment in recurrent cases [11]. Dabrafen is a promising single-agent chemotherapeutic drug against BRAF V600E as a single agent and used as a dual agent alongside trametinib for neck and lung metastatic lesions [12,13]. Inhibitors of the mutated FGFR2 (Fibroblast Growth Factor Receptor-2), ponatinib and regorafenib are specific targeted therapies under research [14]. Sonic Hedgehog (SHH) signalling pathway inhibitors (arsenic trioxide and cyclopamine) and SMO (Smoothened gene inhibitors), asvismodegib and iraconazole, appear to be ineffective in few cases and are in trial for ameloblastoma [15,16]. Targeted therapy against BRAF and LGR5 (Leucine-rich repeat-containing G-protein coupled receptor 5) serves as a novel nonsurgical approach for aggressive types of this lesion [17]. The potential use of MEK (Mitogen-Activated Protein Kinase Kinase) inhibitors are currently being investigated and FGFR inhibitors under investigation [2]. Image guided radiation therapy, helical tomotherapy, intensity-modulated radiation therapy and proton beam therapy are current modified radio-therapeutic techniques used in ameloblastoma with promising results [18].

**Conclusion**

Surgical resection with negative margins is mandatory for curative resection and local recurrences are rare. Hence, early diagnosis and prompt treatment is mainstay in the management of any disease. Novel non-invasive diagnostic and therapeutic modalities improve patient comfort and decreases apprehension. Diagnosis and management of ameloblastoma has various schools of thought and future research can be directed towards non-invasive or minimally invasive diagnostic techniques and targeted therapies.

**References**

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