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Observational Study

Characterization of Tumors of Jaw: Additive value of contrast enhancement and Dual-energy Computed Tomography

Justine *et al*., Contrast-enhanced jaw DECT

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Abstract

BACKGROUND

Currently, the differentiation of jaw tumors is mainly based on the lesion's morphology rather than the enhancement characteristics, which are important in the differentiation of neoplasms across the body. There is a paucity of literature on the enhancement characteristics of jaw tumors. This is mainly because, even though computed tomography (CT) is used to evaluate these lesions, they are often imaged without intravenous contrast. This study hypothesises that the enhancement characteristics of the solid component of jaw tumors can aid in the differentiation of these lesions in addition to their morphology by dual-energy CT, therefore improving the ability to differentiate between various pathologies.

AIM

To evaluate the role of contrast enhancement and dual-energy quantitative parameters in computed tomography in the differentiation of jaw tumors

METHODS

Fifty-seven patients with jaw tumors underwent contrast-enhanced DECT. Morphological analysis of the tumor, including the enhancing solid component, was done, followed by quantitative analysis of iodine concentration (IC), water concentration (WC), Hounsfield units (HU), and normalized iodine concentration (NIC). The study population was divided into four subgroups based on histopathological analysis - central giant cell granuloma (CGCG), ameloblastoma, odontogenic keratocyst (OKC), and other jaw tumors. A one-way ANOVA test for parametric variables and the Kruskal-Wallis test for non-parametric variables were used. If significant differences were found, a series of independent t-tests or Mann-Whitney U tests were used.

RESULTS

Ameloblastoma was the most common pathology (n = 20), followed by CGCG (n = 11) and OKC. CGCG showed a higher mean concentration of all quantitative parameters than ameloblastomas ($p < 0.05$). An IC threshold of $31.35 \times 100 \mu g/cm^3$ had the maximum sensitivity (81.8%) and specificity (65%). Between ameloblastomas and OKC, the former showed a higher mean concentration of all quantitative parameters ($p < 0.001$), however when comparing unilocular ameloblastomas with OKCs, the latter showed significantly higher WC. Also, ameloblastoma had a higher IC and lower WC compared to "other jaw tumors" group.

CONCLUSION

Enhancement characteristics of solid components combined with dual-energy parameters offer a more precise way to differentiate between jaw tumors.

Key Words: Jaw neoplasms; ameloblastomas; Dual-energy computed tomography; iodine quantification; Mandibular Neoplasms; Maxillary Neoplasms

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Core Tip: Quantitative DECT parameters provide a reliable way of characterizing morphologically similar jaw lesions and can serve as a single modality to differentiate jaw lesions based on their appearance and material density concentrations. In addition to providing fast imaging and material decomposition algorithms at about comparable dosage equivalency as compared to traditional CT, contrast-enhanced DECT can potentially alleviate the challenge of discriminating jaw lesions without a biopsy.

INTRODUCTION

Various imaging modalities are available for the evaluation of jaw lesions, the most important being panoramic radiographs, computed tomography, and MRI. The imaging approach towards differentiation of these lesions is mainly based on the lesion's morphology, whether lytic, sclerotic, or mixed; multilocular or unilocular; expansion; and features of aggression [1, 2]. Neoplasms across the body, including solid-cystic lesions, are characterized radiologically on the basis of qualitative and quantitative evaluation of the solid component of the tumor, which forms the major component in providing a differential diagnosis. However, the literature on jaw lesions does not emphasize the characteristics of solid components. This is also because, even though CT is used in the evaluation of these lesions, most often they are imaged without intravenous contrast agents, i.e., using cone beam CT scanners (CBCTs). Here comes the role of contrast-enhanced CT, which makes characterization of the solid component possible and gives important information about the nature and extent of a particular tumor, helping the radiologist to give a possible range of differential diagnoses. Dual-energy CT is an innovative technique that operates based on differential attenuation of tissues when penetrated with higher (140 kVp) and lower (80/100 kVp) energy and combines the CT attenuation-based imaging with material-specific or spectral imaging [3]. This in turn gives the added advantage of characterizing lesions based on the quantitative parameters touted to be material-specific, which can further increase the diagnostic confidence with which the radiologist conveys the possible diagnoses. The hypothesis of this study is that the enhancement characteristics of the solid component of jaw tumors is important for the differentiation of these lesions and evaluation of the same in addition to its morphology by dual-energy CT, therefore, improves the ability to differentiate between various pathologies [4, 5, 6]

MATERIALS AND METHODS

This observational study was conducted prospectively from July 2020 to April 2022 after obtaining approval by the Institutional Ethics Committee (IECPG-354/22.07.2020, RT-2/26.08.2020). The study subjects were patients who presented with complaints of swelling in the maxilla or mandible. Patients were first screened with panoramic radiographs. Those who were found to have any lytic or sclerotic lesions in the panoramic radiographs were included. Patients without histopathological confirmation, those with uncomplicated, typical benign cysts on OPG (such as radicular cysts and dentigerous cysts), clinically insignificant lesions, patients who were unwilling to participate in the study, and those who were diagnosed with other infectious conditions like osteomyelitis, traumatic lesions, or primary tumors in the oral cavity invading the jaw, were excluded. After giving their full informed consent, all patients underwent a contrast-enhanced DECT. Blood investigations were done to evaluate the renal status before administering intravenous contrast agents.

The clinical information collected was patient demographic data (age and gender) through a proforma filled out by the patient, symptomatology (including swelling, pain, bleeding, fever, tooth mobility, trismus, or any other complaints), and their duration.

Contrast enhanced DECT imaging:

Data acquisitions were performed using single-source dual-energy CT in gemstone spectral imaging (GSI) mode with a fast tube voltage switching between 80 and 140 kVp (Revolution CT, GE Healthcare, Waukesha, Wisconsin, USA). Intravenous non-ionic contrast was given at 1.0 mL/kg. Routine soft tissue and bone windows were read. Standard MPR and panoramic reconstructions were made. In addition, two types of images were obtained from the reconstruction of DECT imaging automatically with GSI viewer software (GE Healthcare) for each patient: the iodine-based and water-based material decomposition images (displayed in Figure 1).

Data collection:

Morphological parameters:

The location of the lesion was recorded according to the bone in which it was seen. The parameters that were evaluated for characterization were - size, aggression, expansion, margins, matrix, cortical involvement, mandibular canal status, and relation to teeth, while cortex involvement and soft tissue extension were evaluated for extent. Based on density and locularity, the lesion was broadly divided into four subgroups: lytic unilocular, lytic multilocular, mixed lytic-sclerotic, and sclerotic (Figure 2). Sclerotic lesions were excluded from further quantitative analysis due to the paucity of measurable soft tissue.

DECT parameters:

The regions of enhancement on soft tissue windows were selected in comparison to virtual non-contrast (VNC) images, and ROI was placed on the most enhancing parts as assessed on monochromatic (65 kev) and iodine images. The measurements included the mean value and area of measurement (mm^2). To ensure consistency, all measurements were performed three times at different image levels, and the average values were calculated. For all measurements, the size, shape, and position of the ROI were consistent between the soft tissue images and the iodine-based material decomposition images, as confirmed using the copy-and-paste function. Lesions with at least a soft tissue component of 1 mm^2 were selected for analysis. The iodine concentration (IC) of the lesions was measured (expressed in multiples of 100 $\mu g/cm^3$) from the iodine-based material decomposition (MD) image, and the water concentration (WC) from the water-based material decomposition (MD) image (expressed in multiples of 1000 mg/cm^3) along with the overlay colormap to increase the assessed lesion contrast. The normalized iodine concentration (NIC) was calculated from the ratio of the measured iodine concentration of the lesion (ICL) and the iodine concentration of the ipsilateral common carotid artery proximal to its bifurcation (ICA) *via* the insertion of two ROIs—one in the assessed lesion and the other in the CCA. In addition to the above, an analysis of the cystic component was also made in the unilocular ameloblastomas and OKCs. The parameters recorded were IC and WC.

Histopathology Data-Gold Standard:

Post-biopsy, excision, or curettage, the sampled tissue specimens were reviewed by two consultant pathologists with 10 years of experience in oral pathology. Sections from routine tissue blocks were examined using hematoxylin and eosin staining. The results were documented as ameloblastoma and non-ameloblastoma, along with the individual-specific histopathological diagnosis.

Statistical analysis: The statistical analysis for this study was done using SPSS version 28.0 software. Continuous variables (age, tumor volume, quantitative DECT, and IHC parameters) were all summarized as mean ± standard deviation, and categorical values were summarized as proportions. The comparison of the mean ± standard deviation between the two groups was done using an independent sample t-test. Categorical variables (histopathology data, patient symptomatology, and morphological parameters) were summarized as percentages. A comparison of proportions between the two groups was done using the chi-square test. Since we compared more than two independent groups for the analysis of DECT quantitative parameters, a one-way ANOVA test was performed for variables that showed a normal parametric distribution (mean HU at 65 kev, ICL, WCL) and a Kruskal-Wallis H test for non-parametric variables (NIC). If significant differences were discovered, we conducted a series of independent t-tests and Mann-Whitney U tests to determine the source of the difference. The value of $p < 0.05$ was considered statistically significant. The diagnostic performance was evaluated by calculating the area under the ROC curve (AUC).

The statistical methods of this study were reviewed by Mr. Hem Sati from the Department of Biostatistics, All India Institute of Medical Sciences, New Delhi.

RESULTS

Demographic and clinical characteristics:

Fifty-seven patients (mean age, 37 years ± 17, 26 males, and 31 females) were included in the study. The maximum number of patients was in the age group of 31-40 years (*n* = 14). The most common presenting complaint was swelling, which was seen in 96% of patients (*n* = 55), followed by local pain in 39% of patients (*n* = 22). The majority of the lesions (44%) were present for more than 6 months.

Histopathology results:

In our study, histopathology was used as the gold standard for diagnosing jaw lesions. Twenty (35.09%) of the 57 patients had ameloblastomas, and 37 (64.91 %) had non-ameloblastomas. With 11 cases, central giant cell granulomas were the most common lesions amongst non-ameloblastomas (29.7%). Table I summarizes the histopathological diagnosis of the lesions.

Morphological analysis on CECT:

Of the 57 patients, 42 (73%) had lesions involving the mandible, and 13 (23%) had maxillary lesions, with thirteen patients having two lesions and two of them having three lesions. The morphological parameters were summarized for both ameloblastoma and non-ameloblastoma groups (Table II). The ameloblastoma group showed a higher median volume (73.6 cm^3), more necrosis, a higher percentage of inferior alveolar canal involvement, retromolar trigone involvement, and cortical involvement in the form of expansion or thinning. All these were statistically significant.

Aggressive features evaluated in the case of mandibular tumors included mandibular canal involvement (n = 12), involvement of retromolar trigone (RMT) (n = 16), condyle (n = 2), and coronoid process (n = 3). In cases of lesions in the maxilla, six cases showed aggressive features in the form of extension into the infratemporal fossa/orbit/pterygoid plates. Overall, locally aggressive features were seen in 19 cases (33%).

Quantitative analysis of solid components in contrast-enhanced DECT:

On a broad comparison between the ameloblastoma and non-ameloblastoma groups, the ameloblastomas had a higher mean iodine concentration, a higher mean HU at 65 kev, a lower average NIC, and a lower water concentration compared to the non-ameloblastomas.

The ameloblastomas mostly had iodine concentrations in the 16–30 (moderate) mmol/cu.mm range and mean attenuation in the range of 50–150 HU. In contrast, 90% of CGCGs showed iodine concentrations greater than 31 mmol/cu.mm and mean attenuation >150 HU. The OKCs had low values in all the parameters, distinctly different from others. The rest of them did not show any significant difference between them in their respective groups (Table III). This could be attributed to the heterogeneous sample within the non-ameloblastoma group, which included cystic lesions with virtually no enhancing solid component and avidly enhancing masses. Statistical analysis revealed that the values of DECT parameters in OKCs and CGCCs were on the extreme opposite spectrum, with other lesions having values in between. Hence, we further subdivided the non-ameloblastoma group into three sub-groups and compared ameloblastomas with these three subgroups: odontogenic keratocysts, central giant cell granulomas, and other jaw tumors.

Comparison between ameloblastoma and three major subgroups within the non-ameloblastoma group: (Table IV)

When we compared ameloblastoma and central giant cell granuloma lesions (n = 31), significant differences were found in all quantitative DECT parameters ($p < 0.05$). CGCGs showed a higher average iodine content (36.1 × 100 vs. 29.8 × 100 μg/cm^3), higher average water concentration (1042 x 1000 vs. 1032 x 1000 mg/cm^3), a higher mean HU at 65 Kev (151 HU vs. 122 HU), and a higher NIC (0.59 vs. 0.34) compared to ameloblastomas (Figure 3).

In comparison between ameloblastomas and odontogenic keratocysts (n = 26), both groups showed significant differences in all the DECT parameters. However, the diagnostic dilemma lies in the distinction between unilocular ameloblastomas and OKCs, which appear similar in morphology on conventional CT. Hence, to make this comparison impactful, we compared the water concentration of the cystic component in addition to the DECT parameters mentioned above between unilocular ameloblastomas (UA) and OKCs. Interestingly, in addition to the above quantitative parameters, which were statistically significant, the water concentration of the cystic component also showed statistically significant differences between the two subgroups (Figure 4). In the OKCs, a significantly higher water content within the cystic component was observed compared to ameloblastomas. When the ameloblastomas were compared with the "other jaw tumor" group, the former showed a higher average iodine content, although not statistically significant, and a lower water concentration, which was marginally significant compared to the latter.

ROC analysis for calculating threshold values:

The comparison of ameloblastomas and central giant cell granulomas yielded statistically significant differences and satisfied the sample size for ROC analysis. Hence, ROC analysis for all the DECT parameters was performed, and based on the AUC values, we selected a threshold for each parameter with the largest areas under the ROC curves (Table V).

DECT evaluation of lesions based on morphology:

Because the majority of jaw lesions are diagnosed using a systematic approach based on morphological appearance, we attempted to categorize the lesions based on density and locularity as described above and then studied their DECT parameters, except for the sclerotic lesions. The mean values of the DECT parameters of the lesions in the different morphological subgroups are summarized in Table VI.

DISCUSSION

We performed contrast-enhanced dual energy CT with a predetermined split bolus contrast protocol in 57 patients with suspected maxillary and/or mandibular tumors or neoplasms after obtaining proper written informed consent, reviewing the clinical details, physical examination findings, and orthopantomogram. The morphological and quantitative spectral parameters obtained from DECT imaging were evaluated for the differentiation of various tumors of the jaw. The primary goal of the study was to identify qualitative and quantitative parameters for distinguishing ameloblastomas from non-ameloblastomas.

There was a slight female predominance and majority, i.e., 77% of non-ameloblastomas comprised females compared to 35% in the ameloblastoma group. We studied the morphological features of lesions, and a comparison was made between the amelobalstoma and non-ameloblastoma groups. Median volume, degree of necrosis, inferior alveolar canal involvement, retromolar trigone involvement, and cortical involvement in the form of expansion or thinning were significantly higher in the ameloblastoma group. Our study agrees with these characteristics of ameloblastomas in other studies done previously in larger populations (7-11). However, when the location was maxilla, there was no significant difference between the two groups. The rest of the variables, i.e., margins, relation to teeth, and soft tissue extension, showed no statistically significant difference between the two groups.

In this study, we also investigated the potential of using quantitative information provided by both the virtual monochromatic images and material decomposition images in dual-energy spectral CT imaging for the differentiation of ameloblastomas and non-ameloblastomas. Iodine, as the main component of a contrast medium, allows the assessment of vascular beds and intercellular spaces, and it facilitates the differentiation of lesions at various locations in the body based on the assumption that malignant, aggressive, or vascular lesions exhibit a higher degree of contrast enhancement (12). DECT allows the quantitative assessment of the concentration of iodine accumulated in a unit of tissue volume. The degree of angiogenesis indicates the degree of viability, the degree of malignancy, and the vascularization sources (5,13). Although there were no studies evaluating the role of DECT in jaw tumors, various studies done elsewhere in the head and region showed material decomposition images, especially iodine concentration images, can be used for the differentiation of various pathologies (4). This was because it is now known that the iodine concentration (IC) value is more accurate than the CT value in assessing the blood supply to a lesion.

The higher iodine concentration in ameloblastomas can be attributed to the fact that these are slow-growing, locally invasive tumors with an explicit biologic pattern. Multiple stromal factors, including growth and angiogenic factors, extracellular matrix components, and proteinases, are overexpressed and linked to the development of this tumor, where they play critical roles in invasion, growth, and progression with aggressive behavior. This could explain the rise in metabolic activity in ameloblastoma connective tissue (14-17). The non-ameloblastomas included a heterogeneous sample within the group that ranged from cystic lesions with enhancing wall/septae and virtually no enhancing mural component like odontogenic keratocysts to avidly enhancing solid lesions like CGCGs. This was also supported by the fact that statistical analysis revealed that the values of DECT parameters in OKCs and CGCCs were on the extreme opposite spectrum, with other lesions having values ranging in between. This led to further classification of the non-ameloblastomas and their comparison with ameloblastomas.

On first comparison between ameloblastomas and central giant cell granulomas, the CGCGs had higher mean iodine, water, mean HU at 65 Kev, and normalized iodine concentration (NIC) compared to ameloblastomas. This was in accordance with the earlier studies, which showed that central giant cell lesions had significantly higher angiogenetic potential compared to ameloblastomas [18, 19]. The differential analysis based on the calculated threshold iodine concentration value showed that a value of 32.1 × 100 μg/cm^3, best represented the differences based on the AUC values on the ROC curves, with a sensitivity and specificity of 81.8% and 65%, respectively.

In a comparison of ameloblastomas with odontogenic keratocysts, similar to morphological features, all quantitative parameters showed significant differences between the two lesions in our study (20). Interestingly, in addition to the DECT quantitative parameters of enhancing components, the water concentration of the cystic component also showed a statistically significant difference between the two subgroups. In the OKCs, significantly higher water content within the cystic component was observed compared to ameloblastomas (1020 vs. 997μg/cm^3). Our study showed that unilocular ameloblastomas and odontogenic keratocysts could be effectively differentiated on the basis of the iodine concentration and water concentration measurements of the cystic component, as these lesions are often purely cystic (Fig 4). Our finding that the water concentration of the cystic areas differs significantly between the ameloblastomas and odontogenic keratocysts indicates that the density of the cystic components with suppressed iodine information varies between these odontogenic tumors. Cystic spaces in the ameloblastomas usually contain slightly proteinaceous fluids, occasionally associated with colloidal materials (21). The cyst lumen of odontogenic keratocysts often contains desquamated keratin. This desquamated keratin accumulates in such large quantities that it influences the attenuations on CT images, which was even proven in an experimental study by Yoshiura *et al* (22). Therefore, it is plausible that such desquamated keratin increased the viscosity of fluids in the lumen, thereby increasing the value of water concentration in the water (iodine) images compared with ameloblastomas, in which increases in viscosity may be minimal.

The above comparisons yielded an interesting fact: ameloblastomas showed significantly increased values of DECT parameters, which were indirect markers of vascularity, compared to non-ameloblastomas except for the central giant cell granulomas. As we can see, the latter has a significantly increased iodine concentration, mean HU value, water concentration, and normalized iodine concentration compared to ameloblastomas. The flowchart (Figure 6) presents an algorithmic approach to classifying jaw lesions based on differences in DECT quantitative parameters in our study.

The major limitation of the present study was the heterogeneous sample within the "other jaw tumor" group, which resulted in a limited comparison of separate pathological lesions. Another limitation was the inability to compare the DECT parameters based on the morphological subgroups due to the limited sample size.

CONCLUSION

We propose that DECT can help with both morphological and functional classification of jaw tumors, as well as distinguish between various jaw tumors that closely resemble each other in conventional imaging. Our study contributes to the existing body of literature, confirming the technical feasibility of single-source spectral CT imaging, which relies on the differentiation of iodine and water, as a valuable tool for quantitatively distinguishing ameloblastoma from other jaw tumors at about comparable dose equivalency of traditional CT. Additionally, our research marks the pioneering use of DECT in characterizing and differentiating various jaw tumors.+ADw-/p+AD4APA-/html+AD4-

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