Diffusion-weighted imaging in the evaluation of odontogenic cysts and tumours

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Objective: The differentiation between keratocystic odontogenic tumour (KCOT) and other cystic/predominantly cystic odontogenic tumours is difficult on conventional CT and MR sequences as there is overlap in the imaging characteristics of these lesions. The purpose of this study was to evaluate the role of diffusion-weighted imaging (DWI) and to assess the performance of apparent diffusion coefficients (ADCs) in the differential diagnosis of odontogenic cysts and tumours.

Methods: 20 patients with odontogenic cysts and tumours of the maxillomandibular region were examined with DWI. Diffusion-weighted images were obtained with a single-shot echoplanar technique with *b*-values of 0, 500 and 1000 s mm⁻². An ADC map was obtained at each slice position.

Results: The cystic areas of ameloblastoma (*n*=10) showed free diffusion with a mean ADC value of $2.192 \pm 0.33 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, whereas the solid areas showed restricted diffusion with a mean ADC value of $1.041 \pm 0.41 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. KCOT (*n*=5) showed restricted diffusion with a mean ADC value of $1.019 \pm 0.07 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$. There was a significant difference between the ADC values of KCOT and cystic ameloblastoma (*p*<0.01, Mann–Whitney *U*-test). The cut-off with which KCOT and predominantly cystic ameloblastomas were optimally differentiated was $2.013 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, which yielded 100% sensitivity and 100% specificity.

Conclusion: DWI can be used to differentiate KCOT from cystic (or predominantly cystic) odontogenic tumours.

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A wide range of benign and malignant tumours involve jaw bones, many of which share similar clinical and imaging characteristics. In recent years, MRI has been increasingly used to evaluate cysts and tumours of the oral and maxillofacial region [1]. The imaging features of common lesions like keratocystic odontogenic tumour (KCOT) and ameloblastoma on conventional MRI sequences have been published by many authors [2, 3]. However, there is considerable overlap in the morphological characteristics of these lesions, which make the diagnosis difficult in many cases. In particular, ameloblastomas that are cystic or predominantly cystic are often confused with locally aggressive KCOT. In such cases, precise pre-operative diagnosis can help surgeons to plan treatment, as the therapeutic options are different for these conditions. Diffusion-weighted imaging (DWI) provides an additional paradigm for characterising mass lesions [4]. To our knowledge, only one study has been reported in the literature regarding the use of DWI in differentiating ameloblastoma and KCOT [5]. Therefore we performed this study to evaluate the role of DWI and to assess the performance of apparent diffusion coefficients (ADCs) in the differential diagnosis of jaw cysts and tumours.

Methods and materials

The study was conducted prospectively from January 2009 to October 2010. 35 patients with mandibular cysts and tumours were recruited for a study in our institution comparing the role of multi-detector CT and MRI in jaw lesions. All patients were included after obtaining informed consent, and the study was approved by our institutional ethics committee. DWI was performed in only 24 patients as the technique was standardised during the course of our study. Of these 24 patients, 20 had odontogenic cysts or tumours. This subgroup forms the study population for this article.

MRI was done on a 1.5T MRI scanner (Avanto; Siemens, Erlangen, Germany) using a head coil. *T*₁ weighted axial and *T*₂ weighted fast spin echo (FSE) sequences in multiple planes (axial, sagittal and coronal) were acquired. The parameters for MRI included repetition time (TR) of 600–800 ms and echo time (TE) of 17–20 ms for *T*₁ weighted sequences, and TR=3000–4000 ms and TE=70–90 ms for *T*₂ weighted sequences. The section thickness varied from 3 to 5 mm with a matrix of 256×256. Diffusion-weighted images were obtained with a single-shot echoplanar technique with *b*-values of 0, 500 and 1000 s mm⁻². The parameters used were: TR=4500 ms, TE=72 ms, bandwidth=1735 Hz pixel⁻¹, matrix 128×75; section

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thickness 3.0 mm with 0.3 mm intersection gap, field of view 280–350 mm with the rectangular field of view technique, flip angle 90° and acquisition time 4 min 20 s. Diffusion gradients were applied in all three orthogonal directions separately. Trace diffusion-weighted images and ADC maps were derived automatically on a voxel-by-voxel basis.

Qualitative analysis

The lesions that retained signal on $b=1000 \text{ s mm}^{-2}$ and were hypointense on ADC maps were characterised as having restricted diffusion. The lesions that lost signal on $b=1000 \text{ s mm}^{-2}$ and were hyperintense on ADC maps were characterised as having free diffusion.

Quantitative analysis

The ADC value was calculated manually by placing a circular region of interest (ROI) with minimum area of 1 cm^2 in the lesion.

- For homogeneous cystic (non-enhancing on T_1 weighted post-gadolinium images) or solid (enhancing on T_1 weighted post-gadolinium images) lesions, the circular ROIs were chosen to include the largest possible area of the lesions.
- For heterogeneous lesions with both solid and cystic/necrotic components, the ADC values were measured separately by placing one large circular ROI on the solid and another on the non-enhancing components. Quantitative analysis was not performed if solid or cystic components were $<10 \text{ mm}$ in diameter.

(a)

(b)

(c)

Figure 1. Ameloblastoma in a 42-year-old male patient. (a) Post-contrast T_1 weighted image shows enhancement of the solid component (arrowhead) with non-enhancing cystic areas (arrow). (b) Diffusion-weighted image at $b=1000 \text{ s mm}^{-2}$ shows the solid component has retained the signal (arrowhead) and the cystic component has lost the signal (arrow). (c) The apparent diffusion coefficient (ADC) image shows restricted diffusion in the solid component (arrowhead) and hyperintense signal in non-enhancing cystic component (arrow). The ADC value of the solid component is 1.07 and that of the non-enhancing cystic component is 2.337.

- For every lesion, a mean ADC value was calculated from the ADC measurements of successive slices. The ADC values were expressed as mean $\pm$ standard deviation ($A \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$).

Gold standard

All patients underwent biopsy or surgical resection and histopathological diagnosis was taken as the gold standard for characterising the lesions.

Statistical analysis

The Mann–Whitney *U*-test was used to assess any statistical difference in the ADC values of cystic ameloblastoma and KCOT. A *p*-value < 0.05 was considered to indicate a statistically significant difference.

To assess the diagnostic performance of the ADC value and the sensitivity and specificity of the ADC values for differentiation of the two groups, receiver operating characteristic (ROC) analysis was performed. An optimum cut-off at which cystic or predominantly cystic ameloblastoma and KCOT were distinguished with the highest sensitivity and specificity was determined. All statistical analyses were performed using SPSS software (v. 16; SPSS, Chicago, IL).

Results

Our study included 20 patients with odontogenic tumours and cysts, of whom 10 patients had ameloblastoma, 5 patients had KCOT, 3 patients had odontogenic myxoma and 2 patients had dentigerous cysts.

Conventional MRI sequences in patients with ameloblastoma ($n=10$) showed that the lesions were of mixed

Figure 2. Cystic ameloblastoma in a 35-year-old male patient. (a) Post-contrast T_1 weighted image shows a cystic lesion with capsular enhancement (arrowhead). (b) Diffusion-weighted image at $b=1000 \text{ s/mm}^2$ shows the lesion has lost the signal (arrowhead). (c) The apparent diffusion coefficient (ADC) map shows the lesion is hyperintense (arrowhead), indicating of free diffusion. The ADC value of the lesion is 2.154.

solid and cystic morphology in 5 patients, predominantly cystic in 3 patients and purely cystic with no solid component in 2 patients. The cystic areas were hypointense on T_1 weighted, hyperintense on T_2 weighted and were non-enhancing on gadolinium-enhanced T_1 weighted images. These cystic areas showed free diffusion with a mean ADC value of $2.192 \pm 0.33 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (Figures 1 and 2). The solid areas were hypointense on T_1 weighted images, intermediate to high signal intensity on T_2 weighted images, and showed enhancement on post-contrast images. The solid areas showed restricted diffusion with a mean ADC value of $1.041 \pm 0.41 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (Figure 1).

In patients with KCOT ($n=5$), the lesions were hypointense on T_1 weighted, hyperintense on T_2 weighted and showed enhancement of the walls and septae on post-contrast images. These cystic lesions

showed restricted diffusion with a mean ADC value of $1.019 \pm 0.07 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (Figure 3).

We assessed the utility of DWI in differentiating cystic or predominantly cystic ameloblastoma and KCOT that have overlapping imaging findings on conventional MRI sequences. The ADC values of KCOT and cystic/predominantly cystic ameloblastoma were plotted in box-and-whisker form (Figure 4). When the Mann-Whitney U -test was applied to assess the statistical difference between these two groups, there was a significant difference between the ADC values of KCOT and cystic ameloblastoma ($p<0.01$). The area under the ROC curve was 1.0 for ADC values to differentiate these two groups. From the ROC curve, the optimum cut-off with which KCOT and predominantly cystic ameloblastomas were optimally differentiated was $2.013 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$, which yielded 100% sensitivity and 100% specificity.

Figure 3. Keratocystic odontogenic tumour in a 19-year-old female patient. (a) Post-contrast T_1 weighted image shows a cystic lesion with capsular enhancement (arrowhead). (b) Diffusion-weighted image at $b=1000 \text{ s mm}^{-2}$ shows the lesion has retained the signal (arrowhead). (c) The apparent diffusion coefficient (ADC) image shows the lesion is hypointense (arrowhead), indicating of restricted diffusion. The ADC value of the lesion is 1.019.

Odontogenic myxomas ($n=3$) were hypointense on T_1 weighted images, hyperintense on T_2 weighted images and showed delayed enhancement in two patients (dynamic contrast study was not performed in one patient). These lesions showed free diffusion with a mean ADC value of $2.091 \pm 0.19 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ (Figure 5).

The dentigerous cysts were hypointense on T_1 weighted, hyperintense on T_2 weighted and showed enhancement of the walls on post-contrast images. These lesions showed restricted diffusion on $b=1000 \text{ s mm}^{-2}$, with a mean ADC value of $1.23 \pm 0.09 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$.

Discussion

A variety of benign and malignant lesions involve the jaw bones, and may be odontogenic or non-odontogenic in origin. Ameloblastoma is the most common benign odontogenic tumour, accounting for approximately 11% of all tumours in the jaw [1]. They usually present as a multilocular lesion with mixed solid and cystic components and marked enhancement of solid components, walls and septae. However, 30% of ameloblastomas are unilocular and may be predominantly cystic [1]. Unicystic ameloblastoma, a variant of ameloblastoma that occurs in younger age groups, accounts for approximately 6–19% of all ameloblastomas [6]. These cystic variants of ameloblastomas are often indistinguishable from KCOT on CT and conventional MRI sequences alone. Sumi et al [5] evaluated the role of DWI in differentiating the cystic components of ameloblastomas and KCOT.

DWI, a technique that utilises the measurement of Brownian motion of molecules, is sensitive to physiological parameters such as tissue cellularity, nucleus-to-cytoplasm ratio and integrity of cell membranes [7]. Initially, DWI was applied for the evaluation of intracranial diseases such as cerebrovascular accidents, trauma and epilepsy. Currently, DWI is used for tumour detection, tumour characterisation and to differentiate

neoplastic from non-neoplastic diseases, and is employed in various organ systems [8]. Wang et al [9] first evaluated the role of DWI in head and neck lesions, and found that ADC measurements could be used for characterising these lesions.

In our study, the solid areas of ameloblastoma showed restricted diffusion and low ADC values ($1.041 \pm 0.41 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$), which could be attributed to high tumour cellularity and a greater nucleus-to-cytoplasm ratio. The cystic components showed free diffusion and high ADC values ($2.192 \pm 0.33 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$), which could be attributed to the necrotic contents that are relatively less viscous. A study by Nadal Desbarats et al [10] in differentiating cystic/necrotic glial neoplasms from abscesses supports the fact that necrotic areas of tumours show high ADC values.

The odontogenic cysts like KCOT and dentigerous cysts showed restricted diffusion, which is intuitively unexpected. However, these cysts are different from benign cysts occurring elsewhere in the body. The contents of these odontogenic cysts include glycosaminoglycans, particularly hyaluronic acid [11, 12]. These possibly increase the viscosity of the contents of both KCOT and dentigerous cysts, which probably explains the findings of restricted diffusion and low ADC values in these cystic lesions. The presence of desquamated keratin in KCOT further increases the viscosity of the contents, also contributing to restricted diffusion [5]. However, further studies with biochemical analysis of cyst fluid are required to establish the reason for restricted diffusion in these benign cysts.

When the ADC values of cystic/predominantly cystic ameloblastomas and KCOT were analysed statistically, the mean ADC value of KCOT ($1.019 \pm 0.07 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) was significantly lower than that of ameloblastomas ($2.192 \pm 0.33 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$). This difference in ADC values was possibly due to the difference in the contents of these lesions. These values support the findings of Sumi et al [5] that there is a significant difference between the non-enhancing components of KCOT and ameloblastoma. We found that a cut-off value of $2 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ could differentiate KCOT and cystic/predominantly cystic ameloblastoma with 100% sensitivity and 100% specificity. Sumi et al also reported a similar cut-off value of $2 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$ that differentiated cystic areas of ameloblastoma and KCOT with 91.7% sensitivity and 100% specificity.

Odontogenic myxoma is a benign odontogenic tumour that shows clinical and radiographic characteristics overlapping with other odontogenic lesions such as ameloblastoma and KCOT. The predilection to involve the maxilla more than the mandible and the presence of well-developed internal osseous trabeculae differentiates myxoma from other odontogenic lesions. This tumour is rich in myxoid matrix, which accounts for delayed enhancement with gadolinium. To date, no study has reported the features of odontogenic myxomas on DWI. The myxoid matrix is peculiar in that free water is abundant in extracellular spaces [13]. This explains our findings of free diffusion and high ADC values ($2.091 \pm 0.19 \times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) in these lesions. The study by Maeda et al [13] on musculoskeletal and soft-tissue tumours also showed that myxoid tumours have high

Figure 4. Box-and-whisker plot for comparing the apparent diffusion coefficient values of cystic/predominantly cystic ameloblastoma and keratocystic odontogenic tumour.

(a)

(b)

(c)

Figure 5. Odontogenic myxoma in a 29-year-old female patient. (a) Post-contrast T_1 weighted image shows an ill-defined lesion with heterogeneous enhancement (arrows). (b) Diffusion-weighted image at $b=1000 \text{ s mm}^{-2}$ shows the lesion has lost the signal (arrowhead). (c) The apparent diffusion coefficient (ADC) image shows the lesion is hyperintense (arrowhead), indicating free diffusion. The ADC value of the lesion is 2.122.

ADC values when compared with non-myxoid tumours. Thus DWI may provide an additional paradigm to distinguish odontogenic myxoma from KCOT.

The limitation of our study was the small number of patients. However, these are rare lesions and it is very difficult to get large numbers. We conclude that DWI can be added to the routine MRI protocol with only a small time penalty. This will provide valuable information for differentiating cystic ameloblastoma from KCOT and also in characterising odontogenic myxoma. However, further studies with a larger number of patients are required to validate the role of DWI in jaw lesions.

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