SYSTEMATIC REVIEW

Size distribution and clinicoradiological signs of aggressiveness in odontogenic myxoma—three-dimensional analysis and systematic review

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Objectives: Therapeutic assessment of odontogenic myxoma (OM) is poorly standardized. Unidimensional size criteria have shown to be unreliable in therapeutic decision-making. We evaluate the size distribution of OM and scan for associated clinicoradiological signs of aggressiveness. Additionally, we evaluate three-dimensional size delineation of OM aiming to improve future therapeutic assessment of this destructive neoplasm.

Methods: Primarily, we reviewed the database “PubMed” for data concerning the size of OMs as radiologically determined. Afterwards, the impact of age, sex, locularity and location on the size was investigated by χ^2 test, Student’s *t*-test and regression analysis. Furthermore, we statistically evaluated the impact of size on the occurrence of clinicoradiological signs of aggressiveness. Secondly, we approximated the volume of five unpublished cases of OM by semi-automatic image segmentation of cone-beam CT images.

Results: Multilocular OMs were significantly larger than unilocular ones ($p < 0.002$). Age (0.042) and multilocularity (<0.002) significantly impacted size. Size was significantly associated with cortical perforation (0.032) and multilocularity (<0.002), further regression analysis revealed tooth resorption (0.019), cortical perforation (0.005) and multilocularity (<0.002) as significant predictors of size. Employing the volume as a mean of comparison, we found that the biggest OM (38.42 ml; multilocular) was 124 times larger than the smallest (0.31 ml; unilocular). However, using the maximum diameter (cm) as a surrogate for size, the biggest lesion (6.3) was only 5.25 times larger than the smallest (1.2).

Conclusions: Locularity and volumetric size characterization might help in therapeutic decision-making and could help to improve our understanding of OM.

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Keywords: odontogenic myxoma; size; therapy; volumetric analysis; image segmentation

Introduction

Odontogenic myxoma (OM) is a benign neoplasm of ectomesenchymal origin with aggressive, potentially infiltrative, behaviour and is further defined as “an intraosseous neoplasm characterized by stellate and

spindle-shaped cells embedded in an abundant myxoid or mucoid extracellular matrix”.^{1,2} OM is frequently reported to be the fourth or third most frequent odontogenic tumour.^{1,3–5} This neoplasm originates from tooth-bearing areas of the jaw and is known for invading bone marrow spaces, showing a tendency to relapse after incomplete removal, as cellular neoplastic material can

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persist within small bone marrow spaces.⁶ Average recurrence rate is 25% depending on the treatment, which can be conservative (enucleation, curettage and marginal resection) or radical (segmental, block resection etc.) in nature.^{1,7} Disease recurrence usually occurs within a time frame of 2 years following incomplete removal.¹ However, follow-up should at least be performed for 5 years, as cases of late disease recurrence have been reported.^{1,2}

Therapy is poorly standardized, however, in general, the anatomical extent, as unidimensionally delineated, is taken as a surrogate for aggressiveness and potential to reoccur, helping in therapeutic decision-making. Exemplarily, Boffano *et al*⁸ suggested that conservative treatment could be sufficient for lesions that are smaller than 3 cm in diameter. However, lesions exceeding 3 cm have also successfully been treated by conservative approaches.⁷ Hence, the greatest diameter alone does not seem to sufficiently predict local aggressiveness and thus, the potential to reoccur after conservative treatment.

It is important to note that knowledge about molecular cues that drive neoplastic progression is limited and that a prognostic marker is not available.^{9,10} Knowledge about additional clinicoradiological signs of aggressiveness could be helpful in deciding between conservative and aggressive treatment approaches. Exemplarily, investigations have suggested that multilocular OM are larger than unilocular ones.¹¹ Therefore, we investigate the statistical impact of locularity and other clinicoradiological factors on size, aiming to find factors that could be taken as a surrogate for growth potential and local infiltrative tendency. Furthermore, we aim to evaluate the volume distribution within our series of OM, as three-dimensional analysis, based upon image segmentation, enables a more reliable and accurate assessment of the anatomical extension of a tumour when compared with the maximum diameter.¹² We intend to outline benefits of this diagnostic tool for size characterization of OM which might eventually help in individualized therapeutic assessment.

Methods and materials

Patients

We included all patients, who have been histopathologically diagnosed with an OM by pathology experts and who have consecutively been treated at the Department for Oral and Craniomaxillofacial Plastic Surgery at the University of Cologne between November 2011 and January 2016. All patients received pre-operative digital cone-beam CT imaging. Cone-beam CT scans were taken with the GALILEOS® cone-beam CT device (Sirona, Bensheim, Germany) at 512³ pixels and a resolution of 300 µm or 2.5 line pairs mm⁻¹. Treatment naivety was obligatory as a preceding surgical intervention at the site of volumetric analysis is likely to confound the volumetric data.

Literature review

We conducted a systematic review of the data listed in the PubMed database concerning OM, respecting the “preferred reporting items for systematic reviews and meta-analyses” checklist.¹³ Our search term “odontogenic myxoma” identified 262 publications that have been published between 1 January 1995 and 17 March 2017. Kaffe *et al*¹¹ conducted a systematic review on OM between the years of 1965 and 1995. As we considered available data published within this precise publication, our review presents data on the size of OM taken from investigations conducted between 1965 and 2017.

In the second step, all articles without full-text availability and those written in a language other than English were excluded. A total of 196 articles remained, which were consecutively scanned for data concerning the size of OM as well as associated data concerning the lesion’s locularity, location, the effect on adjacent structures, sex, recurrence and age. For eligibility, strict inclusion criteria had to be met. When the size of the lesion was indicated, it had to be measured in a radiological image, either one, two or three dimensionally. All studies only indicating the size of a pathological specimen were excluded. The lesion’s locularity had to be mentioned or had to be retrievable from radiological images published in the article. In the case of systematic reviews, the exact sources of the data had to be mentioned in order to avoid double entries. It is important to note that some studies measured the diameter of OM in either one, two or even three dimensions. In order to properly merge the data, we chose to uniformly consider the greatest diameter of the lesion as representative of the OM’s size.

Image segmentation, volume approximation and maximum tumour diameter

Background: Image segmentation is roughly the process of labelling voxels of a three-dimensional image grid, allowing voxel-specific delineation of a radiologically visible structure. Based on the number of labelled voxels, this method allows approximation of the segment’s volume. Furthermore, morphometric analysis is possible as the labeled area can be three-dimensionally reconstructed, allowing roundly examination.

The process of image segmentation

For segmentation of OM, we used the open source software ITK-SNAP (Penn Image Computing and Science Laboratory, University of Pennsylvania, Philadelphia, PA, USA).¹⁴ The cone-beam CT DICOM data sets were imported into ITK-SNAP and were demonstrated in sagittal, coronal and axial slices. The intraosseous lesions were identified and delineated with the means of semi-automatic segmentation. Afterward, manual segmentation was performed to control and ensure correct segmentation. The volume of the lesions was computed automatically in cubic millimeters by the program. This is a validated method to

Table 1 Case data of five patients who were surgically treated between November 2011 and January 2016 owing to an odontogenic myxoma of the jaws

Age	Volume (ml) and diameter (cm)	Sex	Location	Locularity	Therapy	Reconstruction of the resulting defect (yes/no)	Recurrence within follow-up
11	38.4 (6.3)	F	Mandible	M	R	Yes	No (17 months)
34	4.7 (2.2)	F	Mandible	M	R	Yes	No (34 months)
41	24.7 (4.1)	M	Maxilla	M	C	No	No (46 months)
51	0.31 (1.2)	F	Mandible	U	C	No	No (32 months)
54	4.9 (3.1)	F	Mandible	M	C	Yes	No (42 months)

C, conservative treatment: enucleation, curettage; M, multilocular; marginal resection; R, radical treatment: segmental or block resection, hemimandibulectomy; U, unilocular.

perform morphometry and volume analysis based upon cone-beam CT imaging in tissue segmentation.¹⁵ This technique is based upon manual, semi-automatic and automatic methods.¹⁶ Regularly, semi-automatic segmentation is performed as it combines the efficiency and repeatability of automatic segmentation and the correct delineation of manual segmentation.¹⁶ The open source medical imaging program, ITK-SNAP, is based upon geodesic active contour and region competition methods and thus, offers manual and semi-automatic tools to analyse the volumes of anatomical regions of interest.¹⁴ The program was initially validated for volumetric and morphometric analysis of the caudate nucleus of the brain. Multiple consecutive studies confirmed these results.^{15,17}

Maximum tumour diameter

With the help of ITK-SNAP, we manually measured the three maximum orthogonal tumour diameters in centimeters (cm) in anteroposterior, mediolateral and craniocaudal direction. Only the greatest of the three orthogonal diameters was used for investigative purposes (Table 1).

Statistical analysis

For statistical analysis, we provide descriptive statistics. Student's *t*-test was used to compare mean values. Statistical analysis of categorical variables was carried out using the χ^2 test. Regression analysis was conducted with the size (greatest diameter) as the dependent variable and locularity, cortical perforation, tooth displacement and tooth resorption as predictor variables. Standardized coefficients (β) and significance levels are provided. The significance level was set to $p < 0.05$. All statistical analyses were performed using SPSS Statistics for Windows (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.).

Results

Systematic review

Concerning the review of literature, we considered 18 publications that were published between 1 January 1995 and 17 March 2017 (Table 2). It is important to note

that the cases published by Peltola et al¹⁸ have already been considered within the study conducted by Kaffe et al.¹¹ However, the investigation provides additional information and is, therefore, listed in table two.

Importantly, only a small number of publications provided full case data containing information about size, sex, location, locularity, effect on adjacent tissue and age. The number of cases that provided full case data is indicated at the bottom of the respective column.

With the help of the weighted arithmetic mean, we found that unilocular and multilocular OM's show a mean diameter of 2.8 and 5.4 cm, respectively. Patients with multilocular lesions tended to be younger with a mean age of 29.5 years (mean age unilocular: 36.3 years). A total of eight investigations provided data concerning the post-operative follow-up period. In only one case recurrence occurred. Treatment was mainly radical in nature.

Statistical analysis

In total, individual case data of 44 patients were available for statistical analysis [Supplementary Table 1 (Supplementary material available online)]. The patient sample showed a mean age of 35 years. The greatest diameter was in mean 4.05 cm (SD 2.4) with a minimum of 0.7 and a maximum of 10 cm. 16 OM's showed unilocularity and 28 multilocularity. A total of 32 lesions was located in the mandible and 12 originated in the maxilla. 7 patients showed tooth resorption, 17 tooth deviation and 23 cortical perforation.

Mean age of females and males was 39 and 29, respectively (Student's *t*-test $p = 0.052$). Additionally, patients showing involvement of the mandible (38) were in mean older than those with maxillary involvement (27) (Student's *t*-test $p = 0.019$). Accessory results of statistical analysis are provided within Tables 3 and 4. Importantly, locularity and age significantly impacted size when comparing mean values (Student's *t*-test, $p = 0.002$ and 0.042 , respectively). χ^2 test revealed that size (>4.05 upper half of mean) was significantly associated with multilocularity ($p < 0.002$) and cortical perforation ($p = 0.032$).

Furthermore, we conducted a regression analysis on the present data with the maximum diameter (cm) as the dependent variable. Predictor variables to be found

Table 2 Review of literature 1995–2017

Author and year	No. of relevant cases (full case data)	No. of UL	No. of ML	Mean age total	Mean size UL (cm)	Mean size ML (cm)	Mean follow-up (range)	Recurrence	Treatment
Kaffe, Naor et al 1997 ¹¹	87 (0)	34	53	29.3	2.7	5.6	NA	NA	NA
Noffke, Raubenheimer et al 2007 ⁶	30 (0)	6	24	31.3	4.3	7.1	NA	NA	NA
Peltola, Magnusson et al 1994 ¹⁸	21 (21) ^a	10	11	^a	^a	^a	NA	NA	NA
Wang, Guo et al 2016 ¹⁹	18 (0)	3	15	35.5	1	3.7	NA	None	R
Friedrich, Scheuer et al 2012 ²⁰	13 (0)	9	4	26.2	NA	NA	NA	NA	NA
Boffano, Gallesio et al 2011 ⁸	10 (0)	2	8	40.1	2.3	4.3	67.3 (12–165)	None	R/C
MacDonald-Jankowski, Yeung et al 2004 ²¹	7 (7)	4	3	35.2	3.7	3	NA	None	NA
Garcia, Campo et al 2006 ²²	1 (1)	1	–	34	2.5	–	NA	None	NA
Spencer and Smith 1998 ²³	1 (1)	–	1	33	–	3	NA	NA	R
Sumi, Miyaishi et al 2000 ²⁴	1 (1)	–	1	48	–	7	22	None	C
Boussault, Boralevi et al 2006 ²⁵	1 (1)	–	1	1.2	–	3.5	NA	NA	NA
Albanese, Nocini et al 2012 ²⁶	1 (1)	–	1	24	–	4.8	NA	None	C
Guo, Li et al 2014 ²⁷	1 (1)	–	1	14	–	6.3	12	None	R
Kiresur and Hemavathy 2014 ²⁸	1 (1)	–	1	17	–	4.9	NA	None	NA
Ram, Mehta et al 2014 ²⁹	1 (1)	–	1	52	–	5	18	Yes	R
DeFatta, Verret et al 2006 ³⁰	1 (1)	–	1	30	–	10	36	None	R
Lahey, Woo et al 2013 ³¹	1 (1)	–	1	69	–	3	14	None	R
Rajasekhar, Mushtaq et al 2009 ³²	1 (1)	–	1	17	–	7	24	None	C
Present study	5 (5)	1	4	38.2	1.2	3.9	22.2	None	C/R
Sum	181 (44)	60	121		<i>N</i> = 51	<i>N</i> = 117	–	–	–
Weighted arithmetic mean	–	–	–	–	2.8	5.4	–	–	–

C, conservative; ML, multilocular; NA, data not available; No., number; R, radical; UL, unilocular.

^aCases are included in the study conducted by Kaffe et al.**Table 3** Statistical evaluation of sex, age, location, impact on adjacent tissue and size of 44 cases of odontogenic myxoma with the help of student's t-test

	Mean ± SD (cm)	p-value
Overall	4.05 ± 2.4	
Sex		
Female	3.6 ± 2.1	0.109
Males	4.8 ± 2.7	
Locularity		
ML	5.1 ± 2.2	0.002
UL	2.3 ± 1.5	
Location		
Mandible	4.1 ± 2.4	0.820
Maxilla	3.9 ± 2.5	
Age		
Upper half of median (>31.5)	3.4 ± 2.1	0.042
Lower half of median (<31.5)	4.7 ± 2.5	
Cortical perforation		
Yes	5 ± 2.5	0.004
No	3 ± 1.8	
Tooth resorption		
Yes	5.8 ± 2.9	0.034
No	3.7 ± 2.2	
Tooth deviation		
Yes	4.1 ± 2.7	0.935
No	4 ± 2.2	

ML, multilocular; UL, unilocular.

statistically significant were tooth resorption (0.019), cortical perforation (0.005) and multilocularity (<0.002) (tooth deviation = 0.980) [standardized coefficients (β): 0.271; 0.342; 0.512; 0.01].

Volumetric analysis, maximum diameter and three-dimensional visualization using image segmentation

Between November 2011 and January 2016, a total of five surgically treated osteolytic jaw lesions turned out to be attributable to an OM. Patient characteristics and volumetric data can be found in Table 1. In detail, the cohort presented a mean volume of 14.71 ml with a SD of 16.3 ml. Furthermore, we found a minimum and maximum volume of 0.31 (unilocular radiolucency) and 38.42 ml (multilocular radiolucency), respectively. One lesion appeared as an unilocular radiolucency whereas four were of multilocular appearance.

The mean maximum orthogonal diameter was 3.4 cm with a SD of 1.9 cm. Minimum and maximum diameters were 1.2 and 6.3 cm, respectively. Employing the volume as a mean of comparison, we found that the biggest OM (38.42 ml) was 124 times larger than the smallest (0.31 ml). However, when using the maximum diameter as a mean of comparison, we found that the biggest lesion (6.3) was only 5.25 times larger than the smallest (1.2).

With the help of image segmentation, we were able to create a three-dimensional model of each OM. Consecutively, we analysed the morphometric characteristics.

Table 4 Cross-classified table to statistically evaluate the association between size and clinicoradiological parameters of aggressiveness in 44 cases of OM

	<i>UL</i>	<i>ML</i>	<i>Cortical perforation</i>	<i>Tooth deviation</i>	<i>Tooth resorption</i>
<i>n</i>	16	28	23	17	7
Size (cm)					
Upper half of mean (>4.05)	1	19	14	10	5
Lower half of mean (<4.05)	15	9	9	7	2
<i>p</i> -value (χ^2)		0.002	0.032	0.651	0.132

ML, multilocular; *n*, number of cases that were assigned to the respective category; UL, unilocular.

Figure 3 CBCT axial slice. Multilocular odontogenic myxoma showing a complex three-dimensional structure with intralésional trabeculation and buccal expansion.

Four out of five patients showed a complex configuration of the osteolytic jaw lesion with wide intramedullary expansion (mandibular OMs) and extension into the maxillary sinus (maxillary OM), multilocularity, great size, cortical perforation and partially tooth deviation and root resorption. One individual showed a rather cystic lesion with clear margins, unilocularity and small size which was considered to morphometrically represent an inconspicuous configuration (Figures 1–6).

Mean follow-up for our patient sample was 34 months. Maximum possible follow-up was reached for four patients (Table 1).

Figure 1 Panoramic radiograph. Multilocular odontogenic myxoma with intralésional trabeculation in an 11-year-old individual with a volume of approximately 40 ml.

Discussion

OM is a benign neoplasm lacking a tumour capsule, showing the tendency to expand into bone marrow spaces (“pseudo-malignant” invasion), thereby, causing osseous destruction and clinically showing a high rate of recurrence when conservatively treated.^{1,2} Incomplete removal of this gelatinous mass is thought to be the mechanism responsible for the high rate of recurrence which is reported to reach up to 33%.³³ However, little is known about molecular cues involved in disease initiation and progression. The exact pathophysiological mechanisms, thus, remain elusive.

Therapeutic decision-making is poorly standardized, mainly because OM is a rare neoplasm and thus, the realization of large single-centre prospective investigations is nearly impossible. The lack of evidence-based surgical guidelines renders therapeutic management of OM difficult. In order to provide guidance, the size of OM frequently serves as a surrogate for its aggressiveness, the tendency to expand and the potential to reoccur. Hence, the decision between conservative and radical approaches frequently depends on the size as indicated by the greatest measurable diameter.^{7,8,34} Exemplarily, Boffano *et al*⁸ have advocated to radically treat those lesions exceeding a maximum diameter of 3 cm. However, lesions exceeding this value have successfully been treated by conservative approaches.⁷ This fact suggests that the greatest diameter alone does not seem to sufficiently serve as a surrogate

Figure 2 Panoramic radiograph. Unilocular odontogenic myxoma without intralésional trabeculation in a 51-year-old individual with a volume of approximately 0.3 ml.

Figure 4 CBCT coronal slice. Multilocular odontogenic myxoma showing a complex three-dimensional structure with intralesional trabeculation and buccal expansion.

for local aggressiveness and thus, the probability of successful treatment with the help of conservative or radical methods.

Consequently, we intended to evaluate the correlation between the greatest diameter and clinicoradiological signs of aggressiveness (cortical perforation, tooth resorption, tooth deviation, recurrence, multilocularity). Multilocular lesions are defined by containing a minimum of two distinct pathological compartments that are divided by intralesional septa.¹¹ Jaw lesions that can show multilocularity are, for example, OM, keratocystic odontogenic tumour, ameloblastoma and central giant cell granulomas.³⁵ Importantly, multilocular appearance was considered as a sign of aggressiveness as previous investigations of keratocystic odontogenic tumours have shown that multilocular lesions are significantly associated with a higher risk of recurrence and greater size when compared with unilocular ones.³⁶ Therefore, we intended to evaluate the relevancy of locularity as a predictor of size and radiological signs of aggressiveness in OMs. Additionally, we investigated whether location, sex and age impact the lesion's size.

Figure 5 CBCT axial slice. Unilocular odontogenic myxoma exhibiting a cystic appearance (left hemimandible).

Figure 6 CBCT coronal slice. Unilocular odontogenic myxoma exhibiting a cystic appearance (left hemimandible).

The aim was to evaluate accessory factors that could potentially, in combination with the lesion's size, serve as a surrogate for aggressiveness and thus, help in applying the correct treatment.

First of all, we found multilocular lesions to be significantly larger in size ($p < 0.002$) when compared with unilocular ones which is consistent with published literature (Table 3).^{6,18,37} In addition to that, age significantly impacted the size of OM ($p = 0.042$). Patients under the age of 31.5 (lower half of median) showed bigger lesions (mean 4.7 cm) when compared with patients over the age of 31.5 (upper half of median) (mean 3.4 cm). Neither sex nor location showed a statistically significant impact on size. Furthermore, lesions showing cortical perforation ($p = 0.004$) and tooth resorption ($p = 0.034$) are in mean significantly larger than those not showing these clinicoradiological factors of aggressiveness. Furthermore, χ^2 test revealed that both multilocularity and cortical perforation significantly impacted size (Table 4). Interestingly, regression analysis further revealed that tooth resorption, cortical perforation and multilocularity are all statistically significant predictors of lesion size when measured in centimeters. Owing to a lack of data, we were not able to investigate the impact of the aforementioned clinicoradiological factors on the rate of recurrence. Only one patient showed signs of recurrence. In total, eight investigations provided data on the follow-up period. Not a single investigation reported on a follow-up of a minimum of 5 years. Hence, as disease recurrence is most likely within this interval, present data do not allow for judgment of therapeutic success as judged by disease-free survival.²

The present results show that the size of an OM (unidimensionally delineated) correlates with multilocularity, tooth resorption and cortical perforation. Lesions exhibiting these signs are more likely to be bigger compared with those not exhibiting these specific signs.

In particular, multilocularity seems to be of high value when wanting to predict the size of an OM as shown by regression analysis.

Based on our findings, that multilocular OMs are significantly larger than unilocular OMs, one could speculate that there might exist two biologically distinct OMs: an unilocular biologically restrictive version and a multilocular biologically more aggressive lesion, resulting in a differential three-dimensional configuration and size (Figures 1–6).

However, other non-neoplasm-specific factors that can influence the size and radiological appearance are widely neglected within this investigation. The size difference between uni- and multilocular lesions might at least partially be attributable to intrinsic bone characteristics of the patients and not only to the neoplastic potential of cancer cells. Factors such as bone marrow density, vascularization and availability of growth factors can influence neoplastic disease progression. Neoplastic cells can be nurtured by the bone microenvironment (“Seed and Soil” theory).^{38,39} It is possible that this fact explains why we found that younger individuals (<31.5 years, lower half of median), putatively with healthy bone marrow and optimal blood and nutrient supply, showed larger lesions.

Additionally, it is necessary to discuss the possibility that multilocular, large-sized lesions are longstanding and the multilocular appearance is the result of a time-dependent degenerative process. This would imply that unilocular lesions present the early stages of OM development. However, present findings do not support this hypothesis. First of all, we were able to find evidence of the existence of large unilocular lesions that partially exceed the size of multilocular ones (Supplementary Table 1). This implies that growth of unilocular lesions takes place, however, not resulting in a multiloculated three-dimensionally complex lesion. Assuming that unilocular OMs present an early stage of neoplastic progression, it is unlikely that there would be unilocular large-sized OMs coexisting with equally sized multilocular OMs.

In order to further investigate unilocular and multilocular OMs, we chose to analyse the three-dimensional configuration of OM in order to evaluate whether multilocular lesions are morphometrically more complex structures. If multilocular OMs are biologically more aggressive, one would expect them to show a higher grade of three-dimensional complexity owing to three-dimensional arbitrary infiltration of bone marrow spaces.

Morphometrically, one can observe that the unilocular OM is quite easily configured, lacking complex three-dimensional intralésional trabeculation, suggestive of a non-neoplastic jaw cyst. The greatest multilocular OM shows high complexity and size (Figures 1–6). This striking morphological difference could be attributable to a differential aggressiveness. It is important to note that the individual with the multilocular, big lesion, was 11 years of age, whereas the unilocular OM

was found in a 51-year-old individual. Complexity, younger age and greater size of the multilocular OM (Figures 1, 3 and 4) could be indicative of a differential genetic program, responsible for neoplastic disease progression and initiation. Owing to small patient sample within this investigation, strong conclusions cannot be drawn. Most importantly, image segmentation and volume measurement, as well as the systematic review, suggest a size difference between uni- and multilocular lesions. It is possible that these radiographically distinct lesions exhibit differential aggressiveness. In this context, investigations of a defining genetic program, responsible for uni- and multilocular OM could be interesting and potentially helpful in further elucidating the pathophysiology of OM. Results might improve our understanding of OM and help in future therapeutic decision-making.

Finally, we intend to discuss the role of image segmentation for delineation of an OMs size. Dejacó *et al*¹² showed that the volumes of smaller neoplasms are particularly overestimated when taking the maximum orthogonal diameter as a surrogate. Hence in this study, we approximated the volume of OMs with the help of image segmentation and aimed to evaluate this method in the context of unidimensional characterization of an osteolytic jaw lesion's size.

Volumetric analysis revealed a great variance in size, ranging from a small lesion with 0.31 ml to a giant lesion with 38.42 ml (Table 1). Interestingly, the smallest lesion (0.31 ml) showed unilocular configuration whereas the other four multilocular myxomas were exceedingly larger, cumulating in a lesion that was 124 times bigger (38.42 ml). Note that the ratio of the maximum orthogonal diameter between these two extremes was 0.2 (1.2/6.3), actually concealing the immense size difference as volumetrically determined. It is possible that volumetric analysis is superior to the maximal orthogonal diameter in accurately delineating an OMs size, thereby, allowing more accurate comparative investigations and therapeutic decisions.

However, small patient sample forbids strong conclusions. Therefore, further investigations focusing on the relevancy of volumetric analysis for correct delineation of an OM's size are necessary. In particular, larger multicentre investigations should be carried out investigating the association between volume and recurrence rate.

Conclusion

Multilocularity, cortical perforation and tooth resorption are correlated with the size of an OM and thus, could be evaluated in the process of therapeutic decision-making. Particularly, multilocularity seems to be indicative of a large sized, three-dimensional complex OM. The role of multilocularity as a predictor of biological aggressiveness needs to be further addressed. Furthermore, image segmentation suggests that the maximum diameter leads to overestimation of the

real size of small OMs. The unreliability of taking the greatest diameter as a guide for therapeutic decision-making could be amenable to this fact. Further

investigations specifically addressing the role of volumetric analysis based on image segmentation for therapeutic decision-making is necessary.

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