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Morphological classification of odontogenic keratocysts using Bouligand–Minkowski fractal descriptors

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ABSTRACT

The Odontogenic keratocyst (OKC) is a cystic lesion of the jaws, which has high growth and recurrence rates compared to other cysts of the jaws (for instance, radicular cyst, which is the most common jaw cyst type). For this reason OKCs are considered by some to be benign neoplasms. There exist two sub-types of OKCs (sporadic and syndromic) and the ability to discriminate between these sub-types, as well as other jaw cysts, is an important task in terms of disease diagnosis and prognosis. With the development of digital pathology, computational algorithms have become central to addressing this type of problem. Considering that only basic feature-based methods have been investigated in this problem before, we propose to use a different approach (the Bouligand–Minkowski descriptors) to assess the success rates achieved on the classification of a database of histological images of the epithelial lining of these cysts. This does not require the level of abstraction necessary to extract histologically-relevant features and therefore has the potential of being more robust than previous approaches. The descriptors were obtained by mapping pixel intensities into a three dimensional cloud of points in discrete space and applying morphological dilations with spheres of increasing radii. The descriptors were computed from the volume of the dilated set and submitted to a machine learning algorithm to classify the samples into diagnostic groups. This approach was capable of discriminating between OKCs and radicular cysts in 98% of images (100% of cases) and between the two sub-types of OKCs in 68% of images (71% of cases). These results improve over previously reported classification rates reported elsewhere and suggest that Bouligand–Minkowski descriptors are useful features to be used in histopathological images of these cysts.

1. Introduction

Cysts are pathological cavities containing fluid or semi-fluid content and lined by epithelial tissue. The diagnosis of jaw cysts is based on histopathology features, firstly to identify to which of the various cyst types a lesion corresponds to (with different origins, behaviour and prognosis), and secondly, to avoid misdiagnosis with other lesions (e.g. as intra osseous squamous cell carcinoma, unicystic ameloblastoma and other tumours) might present with similar radiographical features but require different treatments.

Among the cysts arising in the jaws, two important types are the 'radicular cyst' and the 'odontogenic keratocyst' (OKC). Radicular cysts are the most common type (55% of odontogenic cysts [10]), they are associated with the roots of teeth with non-vital pulps (e.g. due to advanced dental caries) and have slow growth. OKCs are less frequent (12% of odontogenic cysts [10]), they are not associated with dental disease and have certain characteristics common with neoplasms (e.g. active epithelial growth [21,14,15] and higher recurrence rates). Furthermore, there are two OKC sub-types; they can be solitary cysts (sporadic), or they can be multiple (synchronous or metachronous) as part of a rare autosomal dominant disease, the Gorlin-Goltz or Basal Cell Naevus Syndrome (BCNS) [11,20]. About 85% of syndromic and 30% of sporadic cases have mutations of the PTCH1 gene [13], (similarly to basal cell carcinomas of skin) indicating a potential common pathogenesis across OKC sub-types. However, there seem to be differences in the behaviour of syndromic and sporadic OKCs too, and therefore any morphological evidence that could help differentiating between the two sub-types is of diagnostic and predictive importance.

Woolgar et al. [22,23] summarised some histological differences

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between syndromic and sporadic OKCs. While those features are relevant in histopathological terms to understand the organisation of the OKCs, they are difficult to characterise using automated or semi-automated approaches as they require contextual descriptions of cells and tissues that are not directly translated into quantitative features that machine learning algorithms can currently handle. Although an automated technique was proposed to classify other groups of oral cysts in [8], so far in the domain of machine diagnosis the only work addressing the diagnostic differences between syndromic and non-syndromic OKC cysts is [11], where the differences in the morphology of algorithmically segmented cells and the architectural organisation of the epithelial lining of inflammation-free regions of OKCs sub-types were investigated using semi-automated image analysis. Such differences, however, were not sufficient to achieve OKC sub-type classification purposes (60% correct classification rate), although they allowed a good discrimination of OKCs from the most common type of jaw cyst (i.e. radicular cysts) [11]. For expert histopathologists, the latter discrimination should not be a particularly difficult task, but is currently far from becoming automated. Furthermore, the differences between OKC sub-types are more difficult to quantify. If it was possible to rationalise the differences between all these lesions systematically, they could become histolgical discriminators for cases of BCNS, specially in retrospective analyses, in cases exhibiting low penetrance, and to develop indicative markers of recurrence potential. Advances in digital pathology and virtual slides technology have made attractive the possibility of developing machine learning algorithms to help pathologists gather reproducible morphological evidence for diagnostic purposes, to allow analysis of large datasets with multiple tissue sections and to evaluate the results of treatment modalities.

The purpose of this paper is to investigate a statistical approach to the classification of cyst lining images, based on a machine vision algorithm (Bouligand–Minkowski descriptors) that does not require high levels of segmentation of histologically relevant features.

2. Materials

The material used in this paper consists of an anonymised database of 150 images of haematoxylin and eosin (H & E) sections from formalin fixed and paraffin embedded specimens of developmental (solitary and syndromic OKCs) or inflammatory (radicular cysts) origin. Briefly, the database included 65 images of the lining from 13 cases of sporadic (k) OKCs, 40 images from 8 cases of syndromic (s) OKCs and 45 images from 9 cases of radicular (r) cysts (i.e. 5 non-overlapping images per case and with no sectioning artefacts). The cyst types were previously determined by histopathologists using histological as well as clinical information from the respective patients.

The images were captured using an Olympus BX50 microscope (Olympus Optical Co. Tokyo, Japan) with a x40 objective and a colour camera JVC KY-55B (JVC, Tokyo, Japan) attached to a 24 bit RGB frame grabber (Imaging Technologies IT4PCI, Bedford, MA, USA). With this setup the image size was 768×572 pixels with an inter-pixel distance of 0.31 μm. The images were background corrected for illumination uniformity (by means of the transmittance ratio of the specimen with an empty bright field frame), for camera bias (by subtraction of a non illuminated frame) and for camera shot noise (each image was the average of 32 consecutive frames). The extent of the epithelial lining of the lesions was segmented (from the background and connective capsule) by optical intensity thresholding (described below), and further analysis was done exclusively on the pixel values of the epithelial lining. Fig. 1 shows one sample for each group (sporadic OKC, radicular and syndromic OKC).

Finally, all the stained images were converted to grey values, where the in the intensity G of each pixel is obtained from the R, G and B components using the following weighted sum:

$$G = 0.2989*R + 0.5870*G + 0.1140*B \quad (1)$$

3. Method

We investigated the classification performance of the Bouligand–Minkowski (B-M) descriptors developed in [2], to classify the images of cyst linings into their original diagnostic groups k (sporadic OKCs), s (syndromic OKCs) and r (radicular cysts). To our knowledge, this is the first proposal for using a statistical approach to this task, while previous works used morphological features that require more complicated pipelines to guarantee that the generated histologically-relevant features are segmented accurately. The method consists of three steps applied to each image: 1) segmenting the epithelial lining from the background (i.e. empty space of the cystic lumen and the surrounding cyst fibrous capsule), 2) computing the Bouligand–Minkowski descriptors of the lining image and 3) concatenating and submitting such descriptors to a classifier algorithm to predict the original type of cysts they belonged to. Section 3.1 briefly describes the steps involved in the segmentation, whereas Sections 3.2–4 provide the theoretical background on the B-M descriptors.

3.1. Segmentation

The segmentation of the epithelial lining was performed by a combination of colour deconvolution and morphological operations. First, colour deconvolution separated the main colour components of the hematoxylin and eosin stained regions into two channels. The epithelial lining typically showed more intense staining in the haematoxylin channel than the other parts of the sample. The histogram equalization and thresholding of this channel allowed highlighting the region containing the epithelial cells. Finally, morphological filtering (using binary reconstruction) was used to eliminate small features producing a clean image where the largest region closely corresponded to the epithelial lining of the cysts. Fig. 2 illustrates the procedure and each step involved. More details can be found in [11].

3.2. Fractal geometry

A fractal [16] is a set of points embedded in a topological space that exhibits self-similarity (i.e. the characteristic of being exactly or statistically similar independently of the scale of observation). Fractal geometry concerns the study of the properties that are scale-independent and the self-similarity of such objects. The most commonly used property to characterise such objects is the 'fractal dimension'. This describes the rate of space filling of the set with scale and it can be defined through the Hausdorff-Besicovitch dimension, a concept from Measure Theory, which requires some knowledge of the analytical rules that generated the fractal set.

Fractal scale independence implies infinite amount of morphological detail. Real-world natural objects cannot be infinitely complex, yet some degree of self-similarity and complexity is a common feature. Therefore, it is possible to model such objects by means of fractal geometry concepts (e.g. the fractal dimension) even when there are no well-defined analytical rules (as required by Measure Theory) responsible for generating the sets. An alternative approximation to the Hausdorff-Besicovitch dimension consists of measuring some physical property of the object over a range of scales, e.g. with a ruler with measuring unit length ϵ and counting the number $N(\epsilon)$ of units necessary to measure the length of the object. Such abstraction can be extended to any embedding space endowed with a topological dimension D_T by enlarging the length ϵ and recomputing $N(\epsilon)$, to estimate the fractal dimension D:

$$D = D_T - \lim_{\epsilon \to 0} \frac{\log N(\epsilon)}{\log 1/\epsilon}. \quad (2)$$

In practice, the limit is estimated from the slope of a straight line fit to the plot of $\log N(\epsilon)$ vs. $\log 1/\epsilon$. Quantities other than $N(\epsilon)$ can be used to estimate the self-similarity of objects using, e.g., methods such as box-