Fractal Dimensions of Thyroid tumors on Contrast Enhanced Computed Tomograms

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Abstract

PURPOSE: Contrast enhanced computed tomogram (CT) images of thyroid tumors were analyzed to determine if the heterogeneity could be quantified by a fractal dimension.

MATERIALS AND METHODS: Contrast enhanced CT images were obtained after the injection of iodipamide ethyl ester, a vascular marker, into the patient. Nine CT images of the thyroid tumors taken between 1994 and 1995 were used to trace the enhanced inner patterns of the tumors with a pencil allowing calculation of the fractal dimension using the box counting method and the straight line fit method.

RESULT. All traced inner figures of the tumors met the requirements for a fractal analysis because all patterns showed self-similarities. The mean fractal dimensions were significantly different between benign and malignant thyroid tumors.

CONCLUSIONS. Fractal dimension measurement provides a new means to examine the enhanced inner images of thyroid tumors using the box counting method in contrast enhanced computed tomograms. This may prove useful in understanding and quantifying the pathophysiologic changes in thyroid tumors.

KEY WORDS: fractal theory, box-counting method, contrast enhanced computed tomogram, thyroid tumor

INTRODUCTION

Contrast enhanced computed tomography plays an important role in the management of thyroid neoplasms. Specifically, computed tomographic scans are effective for demonstrating the extent and invasiveness of large thyroid tumors, for evaluating the subternal or retrotracheal extension of tumors, and for detecting and localizing metastatic disease or local recurrence. The characteristics commonly used to describe thyroid tumors include the irregularity of the contour, the complexity of the enhanced inner patterns, and the existence of calcification. Although these indices may be recognized on contrast enhanced computed tomogram, it is difficult to distinguish benign from malignant thyroid tumors for the following reasons: a) considerable overlap exists between the border irregularities seen in benign and malignant thyroid tumor, b) the enhanced inner patterns of both benign and malignant tumors are difficult to distinguish, c) the diagnosis of benign from malignant thyroid tumors using computed tomographic characteristics is both qualitative and subjective.

Numerical and quantitative expressions are, however, important to both compare differences and avoid ambiguity when distinguishing benign from malignant thyroid tumors. This article intends to introduce a new method to distinguishing benign from malignant thyroid tumors using numerical and distinctive expressions, while also supplementing the familiar qualitative concepts currently in use to diagnose thyroid tumors with contrast enhanced computer tomogram.

Fractal geometry, as advocated by Mandelbrot, was established as a method of expressing an image of self-similarity, by scale invariance of form or contained subsystems similar in structure to the whole. Fractal geometry is used to characterize and quantify biological structures that are heterogenous and lack a well-defined scale.

According to the terminology of classical geometry we live in a three-dimensional space: a surface has two dimensions, and a line has one dimension, and a point has zero dimensions. Fractal geometry, on the other hand, is recognized by noninteger dimensions (e.g., 1.423 dimension, 2.381 dimension). The value of the fractal dimension reflects the complexity of the image, the higher value being the more complex.

The usefulness of the fractal dimension has been reported in analysis of human electroencephalograms and electronystagmograms. Recently, fractal dimension has been introduced as a method for the quantitative evaluation of radiograms, and was reported to be...
useful in differentiating malignant from benign lesions in mammograms\textsuperscript{19}. The utility of fractal dimension was also demonstrated in describing the spacefilling properties of glial cells\textsuperscript{30} and the renal arterial tree\textsuperscript{32}.

Fractal dimensions may also be correlated with the complexity of the enhanced inner images (spacefilling images) of thyroid tumors on computed tomogram (CT), and may be useful as a method for expressing them numerically. The main purpose of this paper are 1) to present the idea of fractal analysis applied to enhanced thyroid tumors on CT images, 2) to suggest using the fractal dimension as a parameter for the numerical expression of the inner complexity of thyroid tumors and 3) to calculate the fractal dimensions of the enhanced inner patterns of the tumors in the thyroid gland. In this study, the enhanced inner images of the thyroid tumors were only examined because these images could be recognized in detail while the contour of the thyroid tumor was sometimes difficult to discriminate between normal and malignant lesions, especially in situ and in stage I states.

**METHOD**

**Patients**

All patients who underwent to enhanced computed tomography of the thyroid gland in the Department of Otolaryngology at Teikyo University Ichihara Hospital between 1994 and 1995 were selected. Nine patients who underwent thyroid grand surgery were selected as subjects. Their final diagnoses were obtained from pathological examination after surgery. Four of the nine patients were diagnosed to have benign goiters, and five had malignant tumors (four papillary adenocarcinoma, one malignant lymphoma).

**Computed tomography**

Computed tomography of the thyroid gland was performed using the routine method: matrix 512 x 512, joined sections of 5 mm. The patient was placed in a prone position on the table gantry when the contrast medium (iohexol (JAN) 200 ml) was administered via a venipuncture.

**Image tracing**

One image which had good contrast and no artifact in the tumor was selected from the contrast enhanced computed tomogram. The enhanced inner images except for the contour of the thyroid tumors, were traced with a fine pencil\textsuperscript{33}. Care was taken to trace the image in detail as finely as possible because variations of radiographic density have affected the values of the fractal dimensions. All tracing was performed by one medical student without any knowledge of the tumor pathology or diagnosis to rule out personal bias and preconception.

Figure 1 shows the traced figures of the enhanced inner images except for the contour of the thyroid tumors. The "Benign" group showed traces of benign goiters while the "Malignant" group showed malignant lymphoma (top) and papillary adenocarcinoma (bottom).

Fig. 1. Example of traced figures of enhanced inner images of thyroid tumors on CT.

**Measurement of the Fractal Dimension**

The fractal dimensions of the traced figures of the enhanced inner images of the thyroid tumors were calculated using the box counting method\textsuperscript{34}. The box counting method measures the space filling properties of an object at different resolutions by superimposing a grid of increasing size on the planar space of the figure being measured, and counting the number of boxes \( N(e) \) of the grid size (\( e \)) that contain any part of the figure.

The traced figures were too small to estimate the relation between the number of boxes and the grid size. The traced figures were thus magnified four times to easily superimpose the grids and count the number of boxes. One side of the grid from 1 mm to 20 mm in length was applied to the figures and the number of grids containing figures for each grid size was counted. Log-log graphs of the number of grids containing figures against the grid side length were plotted and linear segments were identified using the least-squares method of regression and the gradients of these segments (S) were calculated. Finally, the fractal dimension (D) was estimated as \( D = -S \).
Table 1 Measurement of the enhanced inner figures in the thyroid tumors

<table>
<thead>
<tr>
<th></th>
<th>r</th>
<th>s.e.</th>
<th>Fd</th>
<th>Median</th>
<th>Q.D</th>
</tr>
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<tbody>
<tr>
<td>Benign</td>
<td>1</td>
<td>0.9912</td>
<td>0.2008</td>
<td>1.240</td>
<td>1.268</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.9961</td>
<td>0.1389</td>
<td>1.254</td>
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<tr>
<td></td>
<td>3</td>
<td>0.9984</td>
<td>0.0883</td>
<td>1.276</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.9992</td>
<td>0.0588</td>
<td>1.299</td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>5</td>
<td>0.9943</td>
<td>0.1765</td>
<td>1.356</td>
<td>1.404</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>0.9956</td>
<td>0.1642</td>
<td>1.371</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0.9978</td>
<td>0.1095</td>
<td>1.400</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>0.998</td>
<td></td>
<td>0.0369</td>
<td>1.436</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>0.998</td>
<td></td>
<td>0.0308</td>
<td>1.458</td>
</tr>
</tbody>
</table>

Abbreviations: r = correlation coefficient; s.e. = standard error; Fd = fractal dimension; Q.D. = quartile deviation. The statistically significant difference in the fractal dimension between benign and malignant thyroid tumors was estimated using the Mann-Whitney U test (p<0.01).

RESULTS

Table 1 shows the results of the straight-line fits, the fractal dimensions and the quartile deviations of the traced figures of the thyroid tumors. In all cases examined, straight-line fits were obtained using the correlation coefficient (r) which was obtained for self-similarity and with a standard error (s.e.) which was obtained arbitrarily. The correlation coefficients ranged from 0.9912 to 0.9992 in the benign tumor and from 0.9943 to 0.9998 in the malignant tumor. The standard error ranged from 0.0588 to 0.2008 in the benign tumors and from 0.0308 to 0.1765 in the malignant tumors. Based on the results of the correlation coefficients and the standard errors, the log(N(e)) - log(e) plots were suggested to be in a straight line and the self-similarity of the traced figures was preserved in all cases. All fractal dimensions were thus calculated.

Fractal dimensions of the traced figures of the benign thyroid tumors ranged from 1.240 to 1.299 (median and quartile deviation = 1.268 and 0.041). The fractal dimensions of the traced figures of the malignant thyroid tumors ranged from 1.356 to 1.458 (median and quartile deviation = 1.404 and 0.065). A significant difference was observed in the fractal dimensions between the traced figures of the benign and the malignant thyroid tumors (Mann-Whitney U test P<0.01)

The confidence interval of the fractal dimensions were estimated to be between 1.183 to 1.340 for the benign tumors and between 1.274 to 1.535 for the malignant tumors with a 95% confidence ratio.

DISCUSSION

Although numerous studies have dealt with the fractal nature of organ structure and physiologic function, few have described the methodology for determining the fractal dimension of radiologic images. Kitaoka and Itoh examined the branching pattern of the human airways with the volume of acini by a fractal analysis. These investigators reconstructed images of fixed, sliced lung specimens and calculated the fractal dimensions using the box-counting method. Honda et al. examined the sialographic ductal patterns of the parotid glands by measuring the fractal dimensions using a box-counting method. They determined the range of fractal dimensions in normal parotid glands and compare them with the findings in the same glands within Sjogren syndrome. Caldwell et al. analyzed digitized mammography images by relating the pixel intensities to the heights of the rectangles. Cargill determined the fractal dimension of the power spectrum obtained in radionucleotide liver scans and showed differences between radiopharmaceutical accumulation in normal and abnormal livers.

The studies by Kitaoka and Itoh and Honda et al. and Caldwell et al. evaluated the spatial structure of attenuation values in organs. These studies provided measures of the organ anatomy. Cargill examined the distribution of a radioactive agent throughout the entire organ.

Because the differential diagnosis of the thyroid tumors was important for determining the surgical method and estimating the patient prognosis, the spatial distributions of the contrast medium after
intravenous injection in thyroid tumors on computed
tomograms were chosen for examination. In this
study, the contrast enhanced inner images of thyroid
tumors on a CT were examined instead of the contour
of the thyroid tumor. The contour changes of the
thyroid tumor on a CT were observed only when the
tumor was large (over stage II) and this can lead to
difficulties in the early detection of malignant thyroid
tumors by CT. The enhanced inner images were,
however, observed even when the tumor was a small
in size and classified as stage I.

The thyroid tumor is three-dimensional and thus a
fractal dimension of a three-dimensional structure
would be optimal. However, because of the standard
computed tomogram is a two-dimensional image, a
selected image of the enhanced inner patterns of the
thyroid tumors were considered to be representative of
the three-dimensional thyroid tumor.

The fractal concept requires only one parameter,
the fractal dimension D, in order to characterize the
enhanced inner irregularities of the thyroid tumor, in
contrast to other more familiar concepts of
characterizing thyroid neoplasms (irregularity of the
contour, complexity of the enhanced inner patterns,
and existence of calcification). This study showed
malignant thyroid tumors to have higher fractal
dimensions than benign tumors. While the number of
subjects studied was small (N = 9), the findings of this
study may indicate that malignant thyroid tumors have
a more sharply defined inner structure of high fractal
dimension. Despite the limited number of subjects, a
statistically significant difference was observed
between these two populations. In other words, the
fractal dimension is considered to be useful in
numerical discriminating benign from malignant
tumors with the enhanced inner images in the thyroid
tumors by CT.

In general, it is difficult to distinguish benign from
malignant thyroid tumors simply from a CT image.
The confidence intervals of the fractal dimensions,
however, revealed two distinct groups of thyroid
tumors although a 20% overlap interval did exist. It
follows that the fractal dimension may thus be useful in
differences in the thyroid tumors on contrast enhanced
inner CT images.

Since traced figures of the enhanced images were
used to measure the fractal dimension, the fractal
dimension might be affected by personal variations in
tracing. To overcome this possibility, only one medical
student, who did not know the pathological diagnosis
of the thyroid tumors, drew the enhanced inner images
of the thyroid tumors on CT. However, a study using
several individuals to select and draw the plural slices
of enhanced inner images and to trace one slice should
be performed to quantify any inherent biases.

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