Fractal Analysis of Brain CT Image in Senile Dementia of Alzheimer Type

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Abstract: Brain atrophy in CT images is often found in patients with Senile dementia of Alzheimer type (AD), but occasionally it is not prominent in some patients with symptoms of dementia. On the contrary, some patients with few symptoms of dementia sometimes show a remarkable atrophy in their brain CT. This is one of the reasons why the diagnosis of AD in the early stage is difficult. Therefore, it is very important that we develop an explicit method to measure the atrophy objectively. Fractal analysis is a method to estimate the complexity of morphology. In this report, we applied this analysis to patients with AD and investigated the relationship between the fractal dimension of cortex surface and the score of HDS-R (Revised version of Hasegawa's dementia scale). As a result, we could not find any significant difference between them. Unfortunately, in this preliminary study, further study is needed, but we think that it will be possible to distinguish fine brain atrophy.

Keywords: Fractal analysis, Head CT, Senile dementia of Alzheimer type, HDS-R Brain atrophy

1. Introduction
In recent years, the aging problem is gradually becoming a threat to Japanese society with respect to problems of labor force, the pension plan, and the national economy. The increase of aged people is inevitably accompanied by an increase of senile dementia. The Ministry of Health, Labor and Welfare estimates that the population with senile dementia will be 3,100,000 by the year 2025. Senile dementia of Alzheimer type (AD) is the most common form of dementia. AD also affects almost 10% of individuals aged 65 years or older [1]. Accordingly, it is especially desirable to diagnose and treat AD in the early stage. Usually, brain imaging such as CT or MRI is used to diagnose AD, but findings of images often do not parallel the symptoms of AD. This is one of the reasons why the diagnosis of AD in the early stage is difficult. Therefore, it is very important that we develop an explicit method to measure the atrophy objectively. Fractal analysis is a method to estimate the complexity of morphology.

2. Objects and method
Nine inpatients with senile dementia of Alzheimer type (AD) were chosen from one private psychiatric hospital for this study. The ages of the subjects ranged from 74 to 86 years old (mean±SD=80.6±4.0). We investigated their diagnoses and their score on the revised version of Hasegawa's dementia scale (HDS-R) according to clinical records which a physician in charge had written. Their diagnoses were all AD, except one patient whose diagnosis was senile dementia.

Fractal analysis was conducted as follows. One transverse cross section was chosen from the brain CT image of each patient. In this section, the Sylvian fissure was the most observable. Figure 1 demonstrates this transverse cross section containing the Sylvian fissure. Then the length of the outline of this section was measured by counting the number of standard lengths needed, as shown in fig. 2. We chose five standard lengths of 1mm, 2mm, 3mm, 5mm and 10mm. Therefore this process was repeated five times. As a result, we got a set of numbers corresponding to a standard length. If the relationship between a number and standard length can be written as
$N(r) \propto r^{-D}$,

in which $r$ and $N(r)$ denote standard length and the number corresponding to standard length, respectively, then we can define $D$ as the fractal dimension[2]. Figure 3 shows that this equation was a good approximation to express this relationship between a number and standard length in one patient. The above relationship had statistical significance in all patients.

Figure 1. The transverse cross section in a CT brain image containing the Sylvian fissure.

A nonlinear simple regression analysis was used in calculating the fractal dimension. Spearman’s rank correlation coefficient was calculated to investigate the relationship between the fractal dimension and the score of HDS-R. Furthermore, a quadratic regression analysis was also conducted to examine the same relationship.

![Regression Curve](image)

Figure 3. The regression curve in one patient. The horizontal axis $N(r)$ is the standard length, and the vertical axis $r$ is the number of standard lengths needed to measure the length of the margin of the brain cross section. The regression equation is as follows:

$$N(r) = 177.109 \cdot r^{-1.061}$$

3. Result

Table 1 shows the result of the calculated fractal dimension. The fractal dimension of the subjects ranged from 0.792 to 1.061 (mean $\pm$ SD=0.951$\pm$0.103). Most of them were less than 1.0. No statistically significant correlation was observed between the fractal dimension of cortex surface and the score of HDS-R, as shown in Figure 4.

<table>
<thead>
<tr>
<th>Age</th>
<th>HDS-R</th>
<th>Fractal Dimension</th>
</tr>
</thead>
<tbody>
<tr>
<td>86</td>
<td>22</td>
<td>0.99</td>
</tr>
<tr>
<td>80</td>
<td>12</td>
<td>0.795</td>
</tr>
<tr>
<td>74</td>
<td>13</td>
<td>0.992</td>
</tr>
</tbody>
</table>
The quadratic function was derived from the quadratic regression analysis without statistical significance as follows:

$$FD = 1.0513 - 0.025 \times HD + 0.001 \times HD^2,$$

where FD is Fractal dimension and HD is HDS-R.

**Figure 4.** The correlation between the fractal dimension and the score of HDS-R in one patient. The horizontal axis is HDS-R (HD) and the vertical axis D is the fractal dimension (FD). This regression curve is not a good approximation of the relationship between them, as it lacks statistical significance.

The regression equation is as follows:

$$FD = 1.053 - 0.025HD + 0.001HD^2$$

4. Discussion

The ages of the subjects ranged from 74 to 86 years (mean ± SD = 80.6 ± 4.0). The score in HDS-R of the patients varied from 3 to 22 (mean ± SD = 9.9 ± 6.8). There were various patients. Some patients with a score of 3 or 5 in HDS-R were suffering from severe senile dementia of Alzheimer type (AD) and some subjects with a score of 18 or 22 in HDS-R were suffering slightly from AD.

In this study, no statistically significant correlation was observed between the fractal dimension (FD) and the score of HDS-R (HD). The fractal dimension in most patients was less than 1.0, although the Fractal dimension would be expected to be more than 1.0 because of the shape of the line graph. The straight line, whose fractal dimension is undoubtedly 1.0, is the simplest shape in all the curves. The fractal dimension of the other more complicated curves appears to have a bigger fractal dimension than that of the straight line. However, we got different results described above. What made this difference? Regrettably the reason remains uncertain.

Hirota et al. [3] reported that the fractal dimension can be a quadratic function of HDS-R with good approximation, but we could not find a good approximation.

HDS-R is the revised version of Hasegawa’s dementia scale. This scale is very convenient to estimate the degree of dementia in clinical medicine, and most clinicians in Japan use this scale. The cut-off point of HDS-R is about 20.

This means that the patient with an HDS-R score under 20 is probably suffering from dementia.

However, a clinical diagnosis must be conducted by using various clinical symptoms of the patient with reference to the HDS-R score. Generally speaking, it is difficult to distinguish dementia from mild memory impairment even if the newest neuroimaging modality such as functional MRI, PET, SPECT or NIRS (near infra-red spectroscopy) is used for diagnosis.

Functional MRI is a tool to investigate noninvasively the change in the blood flow in the brain by detecting the change in the magnetic resonance signal during some task [4], [5]. PET (positron emission tomography) is an apparatus to visualize the metabolism of glucose, the receptor on the neuron and cerebral blood flow with high resolution in space by injecting a positron emission radioisotope into the vein [6], [7]. Furthermore, SPECT (single photon emission computed tomography) also provides an image of the blood flow in the brain by
injecting a radioisotope into the vein. Figure 5 demonstrates a decrease of cerebral blood flow in the frontal lobe in a patient with amnesia of personal history. Both of these two methods need the injection of a radioisotope into the body. Therefore they have the problem of exposing the body to radioactivity, and their methods are invasive, intolerant and complicated to operate.

![Figure 5](image.png)

**Figure 5.** SPECT imaging of the brain in a patient with amnesia of personal history. All of these cross sections are transverse. The upper side is the anterior of the brain and the lower side is the posterior. The anterior of the brain is light-colored. This means a decrease of cerebral blood flow in this area.

In a previous PET study[8], [9], it has been found that there is a correlation between the degree in dementia and the glucose metabolism in the total brain.

Some other research using PET has demonstrated that a decrease in cerebral blood flow is accompanied by a decrease in the metabolism of oxygen and glucose. It has also been reported that SPECT could find the same change of cerebral blood flow and metabolism as FDG-PET (PET using $^{18}$F-fluorodeoxy glucose) [10]. One recent study showed that SPECT could distinguish Alzheimer's disease in the stage of mild cognitive impairment from an ordinary person with 86% accuracy by detecting a decrease in cerebral blood flow in the posterior cingulate gyrus and the precuneus [11]. Since in Japan PET is not covered insurance, its use is limited to the purpose of investigation. For this reason, SPECT is more often utilized than PET to diagnose Senile dementia of Alzheimer type (AD).

NIRS is the newest noninvasive modality to measure the change in oxy-hemoglobin and deoxy-hemoglobin concentration on the surface of the brain cortex with the high resolution in time. This method is very convenient and easy to use, compared with PET and SPECT, since it does not need to use a radioisotope.

These modalities which are mentioned above have been used mainly for the functional imaging of the brain.

On the contrary, there is another approach to image the brain. It is a method to reconstruct the morphological image of the brain. This method is usually conducted by MRI, and the way, which is called voxel-based morphology (VBM), is becoming popular in this kind of imaging. Matsuda [12] demonstrated that VBM was an excellent aid to discriminate between AD and a healthy person advanced in years by focusing the concentration of the gray matter in the medial temporal lobe including the entorhinal area.

Although some progress has been made with the diagnosis using the morphological method such as VMA through MRI or the functional imaging by SPECT, PET or functional MRI, in actuality it is nevertheless hard for the clinician to diagnose dementia such as AD, vascular dementia clearly. It has not yet been widely accepted that there could be a relationship between the decrease in volume of the substance of the brain and the degree of dementia. The accuracy on these methods may depend on the site focused on in the brain [13]. The concept of Fractal has been the object of attention of many scientists to give another way to quantify the feature of the figure.

In geometry, the idea of Fractal was advocated by Mandelbrot 1977 for the first time [14]. This concept gives a new aspect to investigate a figure mathematically. Fractal means some fragment. The fractal dimension, which will be described in detail below, has been introduced to this new geometry.

In general, this fractal dimension can be represented as a real number including a fraction and an irrational number. This is the reason why this new concept of the dimension is named Fractal. In
In this sense, the fractal dimension has made the concept of dimension extensive. Accordingly, it has become possible to manage more complicated shapes which conventional natural science has avoided.

A shape which has the feature of self-similarity is typical of Fractal. Figure 6 shows the Koch curve as the representative of Fractal.

![Koch curve](image)

Figure 6. Koch curve. This curve looks very complicated. It is not smooth and cannot be differentiated anywhere. Its dimension is \( \log 4 / \log 3 \). This curve does not have a characteristic length. In other words, there is a similarity between the total and any part of it.

Fractal dimension reflects some kind of complexity of a figure, as in the figure above.

There are many complicated shapes such as a coastline, mountain chain and the branches of a river in the natural world. Especially in the biological world, there are also many similar shapes like the branches of blood vessels and bronchus, the surface of the brain and surface area of plants.

There are some definitions of the fractal dimension. Exactly speaking, it remains unclear whether these definitions are essentially identical with each other, but the famous and representative definition is called the similarity dimension, as follows:

If one figure consists of a similar figure which is reduced \( 1/a \) in scale and the number of the reduced figure is \( b \) and, furthermore, if there is a relationship between them written as

\[
b = a^D
\]

\( D = \log b / \log a \)

then we can define \( D \) as a fractal dimension.

![Fractal dimension](image)

2 = \( 2^1 \), Fractal dimension = 1

4 = \( 2^2 \), Fractal dimension = 2

8 = \( 2^3 \), Fractal dimension = 3

Figure 7. The similarity dimension.

But this definition cannot be applied to a more general figure, and it is not practical to calculate the fractal dimension actually. There are several practical Fractal definitions, as follows:

1. The way to change the scale of measure
2. The way to use the correlation function
3. The way to use the distribution function

In this report, we took the first one. This method is very convenient and simple to calculate and can be applied to wide variety of objects.

Hirota et al. speculated about the reason why the fractal dimension can be a quadratic function of HDS-R with good approximation as follows. He had thought that memory impairment would be accompanied by the dilatation of the sulcus, and, after that stage, the sulcus would become irregular and
branchy and as a result the fractal dimension would be getting increasingly bigger again in the progressive stages of AD, in which the severe behavior disturbances and the severe atrophy in the brain are observed. Our subjects also included patients with the severe dementia accompanied by severe behavior disturbances. However, our result was inconsistent with that of Hirota et al. The reason might be related to some limitation as follows. There are some limitations in this study. One of them is the small number of subjects. The procedure to calculate fractal dimension may also have been inadequate. We used only one transverse slice of the brain CT images in our calculation. Therefore, it would be better to have more than 5 standard lengths and more CT cross sections.

This preliminary study could not lead to a definite conclusion about the fractal dimension of CT images in AD. Dementia, including AD, vascular dementia and dementia with Lewy bodies, are major sources of morbidity and mortality that have an influence on more than several hundreds millions people in the increasingly aging society of developed and developing countries.

Therefore, further study will be needed to confirm these preliminary findings.

References


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