**Signature:** © Pol J Radiol, 2008; 73(4): 16-20

Polish Journal of Radiology
www.PolRadiol.com
ORIGINAL ARTICLE

**Received:** 2008.07.28
**Accepted:** 2008.10.27

# Correlation of volumetric and fractal measurements of brain atrophy with neuropsychological tests in patients with dementive disorders

**Anna Czarnecka[1], Marek J. Sąsiadek[1], Elżbieta Hudyma[2], Halina Kwaśnicka[2], Mariusz Paradowski[2], Jacek Filarski[1]**

[1] Department of General Radiology, Interventional Radiology and Neuroradiology, Chair of Radiology, Wrocław Medical University, Wrocław, Poland
[2] Institute of Applied Informatics, Wrocław University of Technology, Wrocław, Poland

**Author's address:** Marek J. Sąsiadek, Borowska 213, 50-556 Wrocław, Poland, e-mail: mareks@rad.am.wroc.pl

**Source of support:** Grant N518 022 31/1338 (Ministry of Science).

## Summary

**Background:** Brain atrophy is one of the features of the dementive diseases, but also of other neurodegenerative disorders as well as physiological brain aging. The aim of the study was to define the relationship between the brain atrophy measurements and the degree of the severity of dementive process based on the neuropsychological tests (MMSE and Clock Drawing Test).

**Material/Methods:** In 68 patients with diagnosed impairment of cognitive functions due to dementia, neuropsychological tests (MMSE and Clock Drawing Test) and CT studies were performed. On the basis of CT images we evaluated cortical and subcortical atrophy with 3 methods; visual, semiautomatic (volumetric) and automatic method based on fractal geometry calculations; the latter was characterized by very short time of measurements. The correlation between neuropsychological tests and brain atrophy measurements has been assessed using Pearson's correlation test.

**Results:** No statistical correlation was found between the results of neuropsychological tests and measurements of the brain atrophy (both cortical and subcortical) using all three methods mentioned above.

**Conclusions:** Single measurement of the generalized cortical and subcortical atrophy is not correlated with the results of neuropsychological tests. In our opinion, these measurements might be valuable in follow-up of the dementive process to compare progression of the atrophic changes with the changes of the neuropsychological tests results, especially using very quick automatic method, supplemented by local atrophy measurements.

**Key words:** dementive diseases • brain atrophy • computed tomography • volumetry • fractal

**PDF file:** http://www.polradiol.com/fulltxt.php?ICID=874002

## Background

Atrophy of the brain is associated with physiological aging, but also with degenerative diseases of the central nervous system, including dementive disorders. The increasing average age of the societies in developed countries results in increased frequency of dementive diseases, which gradually become a serious social and medical problem. Therefore efforts are taken to improve effectiveness of diagnosing dementia as early as possible, and thus enable early treatment [1].

Practically, the first diagnosis of dementive disorders is based on the results of clinical examination and neuropsy-

chological tests of cognitive impairment such as MMSE (*Mini Mental State Examination)* and Clock Drawing Test. This is followed by other examinations, including computed tomography (CT). The aim of CT is to rule out the reversible causes of dementia (e.g. brain tumor, normal pressure hydrocephalus, extensive ischemic changes) and to assess brain atrophy. It is essential to define whether the brain atrophy detected in the patient is caused by normal aging, by dementive disease or by overlapping of both processes. Therefore attempts are made to establish precise and reliable quantitative methods, which could answer this question [2–5].

The aim of the study was to define the correlation between the brain atrophy measurements using three methods (visual, semiautomatic and automatic) and the degree of the severity of dementive process based on the neuropsychological tests (MMSE and Clock Drawing Test).

## Material and Methods

The study included 68 patients (48 females, 20 males), aged 45–89 yrs, in whom clinical examination and neuropsychological tests confirmed cognitive impairment, compatible with dementia (42 Alzheimer's disease, 12 Vascular Dementia, 14 Mixed Dementia). In all patients CT with two-row spiral unit (Dual HiSpeed/GE Medical Systems) was performed.

Neuropsychological tests included Mini Mental State Examination (MMSE) and Clock Drawing Test [6]. The former test reflects the general level of cognitive functions based on orientation, memory, verbal, written and other tasks. The result below 24 points (maximal result is 30 points) suggests dementive process. Clock Drawing Test, which evaluates visual space and abstract functions, is based on the task of drawing the clock showing 2:45 hours. In the modification of this test used in this study the maximal impairment of cognitive disorders was evaluated 5 point, while the minimal one – 1 point.

CT studies were performed using 7 mm-thick slices (4 mm in posterior fossa) parallel to supraorbitomeatal line, covering the whole intracranial space.

In evaluation of the brain atrophy we applied three methods:
1. Visual assessment by an expert radiologist.
2. Semiautomatic method, using volumetric software of CT unit, corrected by the radiologist.
3. Full automatic method, using the new method of segmentation, based on fractal geometry.

In all three methods the infratentorial space was excluded to avoid bone artifacts.

### Visual assessment by the expert radiologist

CT images were first assessed visually by the experienced radiologist in order to evaluate roughly cortical and subcortical atrophy, taking into account the patient's age and to rule out other lesions, which could explain the patient's symptoms. Visual assessment was based on the analysis of the source images, with classification of the atrophy in 0–3 scale, where 0 means no atrophy (normal appearance for age), 1 – slight atrophy, 2 – moderate atrophy and 3 – severe atrophy.

### Semiautomatic method

In the semiautomatic source images of the brain were transferred to the workstation of a CT unit. The radiologists selected range of density in Hounsfield units (HU), close to the density of cerebrospinal fluid (CSF) for the regions of interest in the supratentorial space. The authors chose the range from –5 to +20 HU. In the next stage the radiologist corrected the areas found by computer by manual outlining the borders of the anatomic structures. Correction must be performed on each section, separately for extracerebral areas of CSF (cortical atrophy) and intraventricular space (subcortical atrophy). In the last stage, after confirming the labeled regions of interest the volume of both spaces (taking into account the thickness of slice) is calculated by volumetric program in ccm.

### Fractal method

The method is fully automatic and it is performed in two stages: in the first one every image of a CT axial slice is treated as a bitmap in the gray scale. A special algorithm of segmentation is applied to find the cerebrospinal fluid area. This algorithm is based on the hue and placement pixels in the original image. The result of the first stage of the method is a two-coloured image where the only object on is the cerebrospinal fluid. The goal of the second stage of this method is to find the best measure of this object shape.

The fact that the brain, like other organisms and real-world phenomena, exhibits fractal properties, can often be useful for calculating the fractal dimension of a set of sampled data [7]. The fractal dimension measures cannot be derived exactly but must be estimated as the fractal characteristic, which is the real number and defines the level of the object complexity as well as other properties of the space such as area or volume.

In this study we used the most popular and universal method - box-counting dimension known as Minkowski-Bouligand dimension [8]. It is useful even for nonfractal objects. We cover the plane with the regular grid of the size S. N(S) denotes number of boxes in which there is any piece of the fractal. Then we scale down the size of the grid and again calculate $N(S_{next})$.

The box-counting dimension is:

$$D=(\log(N(S_{n+1}))-\log(N(S_n)))/(\log(1/S_{n+1})-\log(1/S_n))$$

Where N(S) – the number of boxes with fractal for the grid size S,

$S_{n+1}$ – the next grid of size $S_{n+1} < S_n$

The performing the fractal method lasted few minutes and was much shorter than in semiautomatic method.

The schematic presentation of the design of our research is shown on the Figure 1

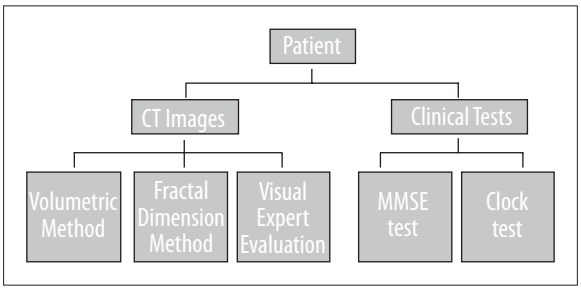


**Figure 1.** Schema of the experiment.

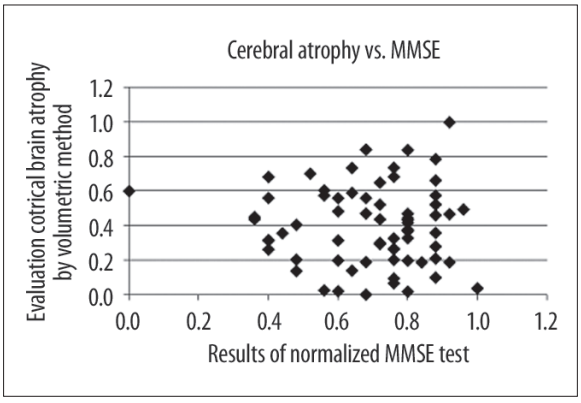


**Figure 2.** The scatter plot shows relationship between evaluation of cerebral atrophy by volumetric method and results of the MMSE test.

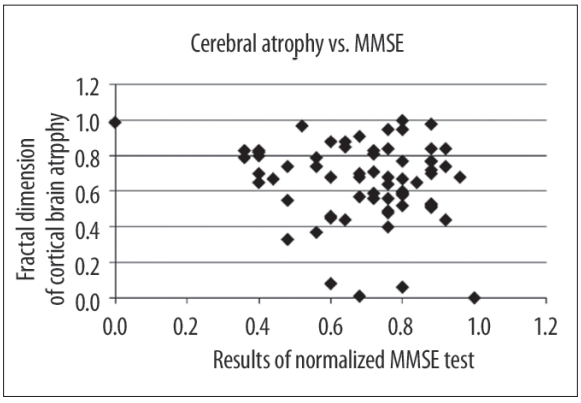


**Figure 3.** The scatter plot shows relationship between fractal dimension of cerebral atrophy and results of the MMSE test.

## Results

In our experiment we obtained a set of data for every patient. Evaluation of atrophy with clinical results of functionality was compared separately for cortical and subcortical atrophy. The aim of the comparison was to check the correlation of the degree of brain atrophy with the results of MMSE and Clock Drawing Tests.

In evaluated group of patients the result of the MMSE test ranged from 0 to 23 and Clock Drawing Test from 1 to 4.

The expert classification of the atrophy was in 0–3 scale.

The volumetric values were real numbers in the range {0.7–20.3} and represented the values of the cortical and

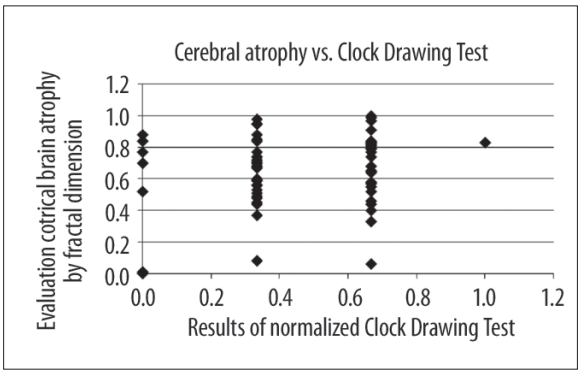


**Figure 4.** The scatter plot shows relationship between evaluation of cerebral atrophy by volumetric method and results of the normalized Clock Drawing Test.

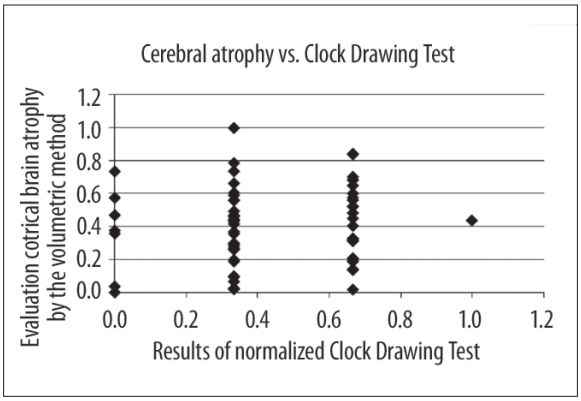


**Figure 5.** The scatter plot shows relationship between fractal dimension of cerebral atrophy and results of the normalized Clock Drawing Test.

subcortical regions of interest containing CSF, referred to the volume of the intracranial supratentorial space.

Fractal dimension calculated for the interesting areas was a real number in the range {1.1–1.8}.

To make the comparison easier, all the values have been normalized to the range {0–1}.

We checked an assumption that measurement of cortical and subcortical atrophy by either method is correlated with neuropsychological tests. On the *scatter plot* drawings (Figures 2–5) every couple of values as Cartesian coordinates is a point in the plane. The pattern of the points allows to estimate the function between the values. The function is calculated by the least square method and shown on the plot. For example the plots below show relationships between various evaluations of cortical brain atrophy and results of the functional tests (MMSE and Clock Drawing Test (Figures 2–5).

A measure of force of matching the two elements in the couple is correlation coefficient ρ, and its estimation from the sample of population r is determined as Pearson coefficient.

The correlation coefficients for the couples of characteristics are presented in the Table 1. The results are based on the research of 68 patients and are presented separately for the cortical and subcortical atrophy (Table 1).

**Table 1.** The correlation coefficients for the cortical and subcortical atrophy between the clinical diagnosis.

| | Visual expert evaluation | | Fractal dimension | | Volumetric coefficient | |
|---|---|---|---|---|---|---|
| | Cortical atrophy | Subcortical atrophy | Cortical atrophy | Subcortical atrophy | Cortical atrophy | Subcortical atrophy |
| MMSE test | –0.07265 | 0.007422 | –0.19378 | 0.044799 | –0.04337 | 0.044714 |
| Clock test | 0.073215 | –0.00395 | 0.19774 | 0.091977 | 0.090238 | 0.116869 |

On the significance level of 0.05, sample size of 68, the critical value $r_{0.05;66}$ is equal to 0.250. Because $|r| < r_{\alpha,v}$ there are no significant statistic relations between cortical and subcortical atrophy evaluated by any of presented methods and any of presented neuropsychological tests.

## Discussion

We evaluated the correlation of brain atrophy in CT studies with the severity of dementia measured in neuropsychological tests using visual assessment and two quantitative methods.

The first, volumetric method, requires the great part of expert radiologist knowledge at every stage of performing:

- Preliminary defining of the range of density in HU to label the region of interest using the volumetric software.
- Visual assessment of the compatibility of the areas labeled by computer program with the borders of the anatomical borders in CT study.
- Correction of the borders labeled by the program by manual outlining the structures or widening the range of density on each section to fit the labeled areas to the anatomical structures.
- Calculation of the volume of labeled areas by the computer program (separately for subcortical and cortical atrophy).

The process described above is very time consuming (up to 2.5 hours) which hampers its application in clinical practice.

The second, fractal method is very quick, needs no human interference and relies on automatic implementation algorithms:

- Preprocessing of the CT images depends on authors' algorithms of segmentation such spaces as cerebrospinal fluid (CSF)
- Calculation of fractal dimension the objects finding into previous stage. It is box-counting dimension which is presented in the previous paragraph.
- Calculation of the mean value of fractal dimension for the all axis slices of the patient.

Both visual assessment and the volumetric and fractal measurements did not show significant correlation with the results of MMSE and Clock tests. However it should be stressed that in both volumetric and fractal methods generalized cortical and subcortical atrophy was evaluated, while, as it is suggested by many authors, the local neurodegenerative changes, e.g. in medial temporal lobes are responsible for cognitive disturbance [9,10].

The lack of correlations mentioned above may support the thesis that cognitive impairment results rather from functional than structural disturbance. The correlation between functional examinations and MMSE test has been described in the studies based on single photon emission computed tomography (SPECT), positron emission tomography (PET), magnetic resonance spectroscopy (MRS) as well as perfusion computed tomography (pCT) [11–14].

The other explanation of our results is a possible overlapping of the cortical and subcortical atrophy associated with normal aging and caused by degenerative process [15]. On the other hand the obtained results might be caused by heterogenity of the analazed groups (patient with different types of dementia). However the aim of the study was to evaluate correlation between the degree of atrophy and severity of cognitive functions disturbance, regardless of the dementia type.

Lack of significant correlations could be also caused by the fact that we analyzed general cerebral atrophy (cortical and subcortical) and not the local atrophy in specific locations.. It resulted from the limited possibilities of the method we have used.

The follow-up evaluation of the degree of atrophy could be possibly more reliable in the assessment of the severity of dementia. As it was already noticed in one of the first long-term studies based on CT measurements [16] the initial volume of the ventricular system did not predict cognitive deterioration and enlargement of the ventricular volume, which was revealed during follow-up.

We believe that long-term prospective studies which enable monitoring of the CSF and brain volumes in individual patient for many years, will be better correlated with severity of dementia, including neuropsychological tests. Introduction of fully automatic, fractal method of the evaluation of brain atrophy would allow to perform such prospective studies and to assess the correlation between the progression of the atrophic changes and worsening the results of the neuropsychological tests. The quick, easy to repeat fractal method could be also used to assess the effectiveness of therapy, i.e. whether it influences only neuropsychological tests or inhibits the progression of brain atrophy as well.

## Conclusions

1. There is no correlation between the degree of generalized cortical and subcortical brain atrophy and the results of neuropsychological tests in patients with dementia.

2. Supplementation of the analyzed methods by possibility of measuring local atrophy should be considered to verify the above conclusion.

3 Short time of evaluation of cortical and subcortical atrophy is a great advantage of the automatic fractal method, which could be therefore used for monitoring the progression of the atrophy changes and its correlation with the changes of cognitive functions measured by neuropsychological tests.

## References:


1. Ritchie K, Lovestone S: The dementias. Lancet, 2002; 360: 1759–66
2. Fox NC, Schott JM: Imaging cerebral atrophy: normal ageing to Alzheimer's disease. Lancet, 2004; 363: 392–94
3. Frisoni GB: Structural imaging in the clinical diagnosis of Alzheimer's disease: problems and tools. J Neurol Neurosurg Psychiatry, 2001; 70(6): 711–18
4. Chételat G, Baron JC: Early diagnosis of Alzheimer's disease: contribution of structural neuroimaging. Neuroimage, 2003; 18(2): 525–24
5. Gołębiowski M: Zespoły otępienne. In: Walecki J (ed.): Postępy neuroradiologii. W: Polska Fundacja Upowszechniania Nauki, Warszawa, 2007; 247–64
6. Kotapka-Minc S, Szczudlik A: Otępienie. W: Rozpoznawanie i leczenie otępień. Wydawnictwo Czelej, Lublin, 2006; 11–22
7. Walecki P, Trąbka J: Miary fraktalne w neuroobrazowaniu. Sztuczna inteligencja w inżynierii biomedycznej. Kraków, 2004; 1–4
8. Peitgen HO, Jurgens H, Saupe D: Chaos and Fractals: New Frontiers of Science, parts I and II (in Polish). Warsaw, PWN, 1995
9. Pantel J, Schröder J, Schad LR et al: Quantitative magnetic resonance imaging and neuropsychological functions in dementia of Alzheimer type. Psychol Med, 1997; 27(1): 221–29
10. Jani J, Prettyman R, Aslam M et al: A retrospective study of neuroradiological abnormalities detected on structural magnetic resonance imaging of the brain in elderly patients with cognitive impairment. Int J Geriatr Psychiatry, 2000; 15(11): 1054–60
11. Kawano M, Ichimiya A, Ogomori K et al: Relationship between both IQ and Mini-Mental State Examination and the regional cerebral glucose metabolism in clinically diagnosed Alzheimer's disease: a PET study. Dement Geriatr Cogn Disord, 2001; 12(2): 171–76
12. Tsolaki M, Sakka V, Gerasimou G et al: Correlation of rCBF (SPECT), CSF tau, and cognitive function in patients with dementia of the Alzheimer's type, other types of dementia, and control subjects. Am J Alzheimers Dis Other Demen, 2001; 16(1): 21–31
13. Waldman AD, Rai GS: The relationship between cognitive impairment and *in vivo* metabolite ratios in patients with clinical Alzheimer's disease and vascular dementia: a proton magnetic resonance spectroscopy study. Neuroradiology, 2003; 45(8): 507–12
14. Zimny A, Leszek J, Kiejna A et al: Analysis of correlation between the degree of cognitive impairment and the results of perfusion CT in patients with dementia. Med Sci Monit, 2007; 13(Suppl.1): 23–30
15. Du AT, Schuff N, Kramer JH et al: Higher atrophy rate of entorhinal cortex than hippocampus in AD. Neurology, 2004; 62(3): 422–27
16. de Leon MJ, George AE, Reisberg B et al: Alzheimer's disease: longitudinal CT studies of ventricular change. Am J Roentgenol, 1989; 152(6): 1257–62