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THE FRACTAL APPROACH AS A TOOL TO UNDERSTAND ASYMPTOMATIC BRAIN HYPERINTENSE MRI SIGNALS

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Abstract

The prevalence of a Patent Foramen Ovale is described in merely 30% of the asymptomatic population. This patency has been shown to be an increasing risk factor for paradoxical cerebral embolization. Some desaturation or decompression situations in human activities such as scuba diving or altitude flight are prone to provoke embolisations. The association with the presence of a patent Foramen Ovale and the onset of cerebral decompression sickness seems to be presenting an odds ratio value of about 5.1.[1] The presence of asymptomatic brain lesion-like "spots" has been investigated in a randomized population of diving individuals ($n = 42$ randomized out of 200). The inclusion criteria were drastic and included: age (less than 41 years of age); diving experience (more than 200 logged dives); no decompression sickness episodes; no contraindications for the MRI examination; and no known central nervous system conditions. Data of the magnetic resonance investigation of the brain has been performed in 42 (diving) volunteers fully informed on the experimental procedures. The statistical comparison (Anova test after Kolmogorov-Smirnov compatibility testing and Neuman–Keuls discriminant post-test) of

the fractal dimension obtained by means of the box counting method with the slope analysis (Harfa fractal analysis program). The comparison was performed with known pathological images such as multiple sclerosis (a pathology not emerging from vascular problems), ischemic thrombotic lesions (vascular problem), diver's asymptomatic brain spots, and the arteriography of the internal carotid in non-pathological humans (clearly vascular). The statistical difference ($p < 0.001$) between the vascular related images, as well as the absence of statistical difference ($p > 0.05$) with the non-vascular spots images advocates with a non-vascular origin of the diver's asymptomatic spots and thus the link between the patency of the cardiac Foramen Ovale and the brain "spots" seems not to be as clear as it was believed.

Keywords: PFO; Long Term Adverse Effects of Diving; MRI; Fractal Analysis; Diving; Decompression.

1. INTRODUCTION

Since 1989, the first publication that spoke about the possible correlation between the presence of a Patent Foramen Ovale (PFO) and the occurrence of decompression Sickness (DCS),[1] there has been no respite in the quest about the possibility of such a relationship. Since 1996, the research department of DAN Europe set out to investigate and respond to a serious concern at the time as a result of this alarming article: "Is there really an increased risk of DCS for a diver who has PFO?"[2–4]

The decompression bubbles are found primarily in the veins; in the heart they are mainly found in the superior and inferior vena cava. Frequently, divers regard PFO as a hole that allows the continual passage between the right atrium and the left — the arterial part of the heart where we do not want to see bubbles (see Fig. 1). The flow coming from the superior vena cava has to pass over a fold, providently given by Nature before touching the PFO (or the Fossa Ovalis).

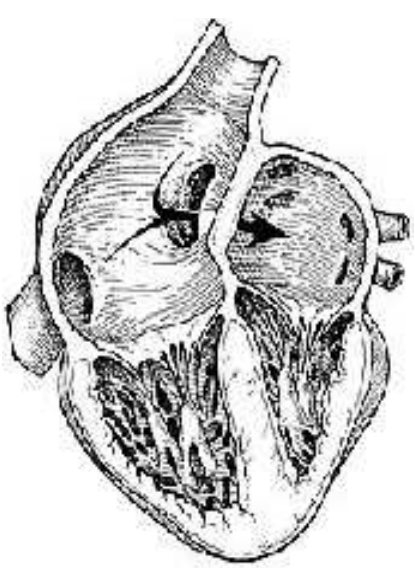

Fig. 1 As a reminder of the interatrial patency during our fetal life (The Foramen Ovale), the Fossa Ovalis is still present in adult hearts. This Fossa Ovalis can be patent and thus is still named Patent Foramen Ovale in about 30% of the normal population.

This causes a sudden increase in the rate of the flow which meets the flow coming from the inferior vena cava and thus turbulence is caused which causes the bubbles to be taken away from the interatrial septum. Therefore if we understand correctly, the bubbles will not cross the Foramen Ovale in natural conditions. But then why are there injections of bubbles made during the transesophageal echocardiogram to measure the PFO, how could they pass in the left atrium? The reason is that respiratory movements are made to reverse the intracardiac flow caused by variations in the intrathoracic pressure.

2. SPOTS ON THE BRAIN AND PFO

A number of years ago, some studies declared the relationship between PFO and cerebral "lesions".[4,5] Since then others have found that there was not a direct relationship.[6,7] In all of these studies, however, we encounter the same population bias. In a previous study, DAN therefore asked two groups of people to sit a test of nuclear magnetic cerebral resonance imaging: 42 were divers and 36 were non-divers. All of the participants had to be under 41 years old because according to previous studies, spontaneous cerebral lesions can occur after 45 years. The distinguishing feature was that this population was randomized. We asked the divers to declare that they had never

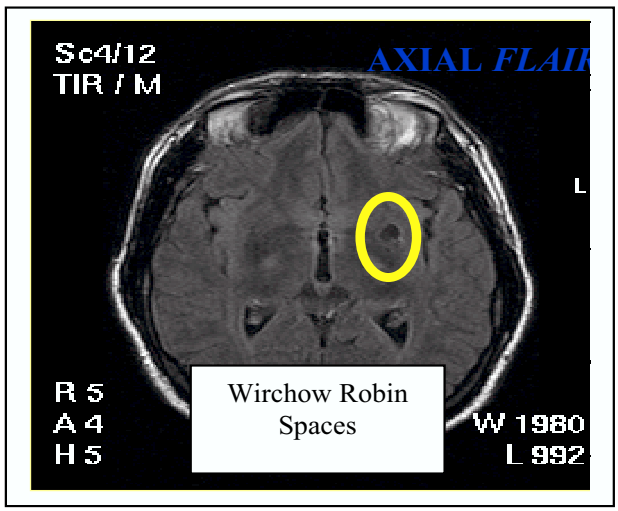

Fig. 2 Typical view of a Wirchow robin Space with the flair filtering; this is not an abnormal brain spot image

suffered from DCS. However, often certain accidents and cerebral incidences in particular, were not declared because of benign or brief symptoms. How many divers have indeed felt a little dazed after a dive ... which goes away after a few minutes ... a case of badly equalized ears or a transient cerebral bubble?

To avoid this situation of poor choice of population we took the case of one diver in four (at the end 42 could finally be tested because, in top of the MRI investigation every diver had to undergo a transesophageal echocardiography to detect the patency of his Foramen Ovale). Then we made a comparison between the numbers and the size of the "spots" found among the divers and those found among the divers and non-divers.

A little more spots were detected among the divers but there was not significantly more ($p > 0.05$). This is contrary to what some authors say with populations that are not randomized and without a control group. Also, to ensure accuracy in the results, a particular imaging filter which allows a reliable diagnosis of the flair sequence to be made was used. Another pitfall that was present was the possibility of finding naturally lacunar zones known as the Wirchow-Robin spaces and diagnosing them as "lesions" (see Fig. 2).

The use of fractal analysis is a known technique in clinical science and particularly in pathology.[8–13] The interesting predictive opportunity of fractal analysis in breast cancer[14–18] or osteoporosis[19–22] is related in pattern differentiation on the medical diagnostic images.

The important possibility of diagnosis before the rise of real objective or clinical symptom is of paramount interest in the medical field. The precise use of fractal analysis in neuroimaging is a moving field with a very promising future. The study of white matter hyperintense signals has been analyzed with the fractal approach in geriatric patients to see if some links can be considered with the white matter hyperintense "spots" and the epileptic seizures.[23]

To our knowledge, nothing has been done to investigate some relations between the significant difference of the fractal dimension of some hyperintense white matter spots in the brain and their spatial distribution in the young patient.

We tried to use the self-similarity concept of the fractals as this has already been used to mark differences between architectural[24–26] or even cancerous structures.[27].

Our aim was to verify if the fractal dimension of some cerebral vascularization images was compatible with the fractal dimension of the asymptomatic brain spots in divers who never experienced decompression diseases or PFO-related headaches.[28–30] All these criteria were included in the population selection criteria.

To calculate the fractal dimension of the images, we used the Harfa 4.0 program applying the box counting method after appropriated filtering and thresholding, and accepting the final result as the fractal dimension — the better occurrence of the slope described in the slope analysis option.

3. METHODS

Our population consisted of a group of 42 healthy divers (scuba divers) not older than 40 years. This population was randomized from a larger population of 200 voluntary divers drastically selected by very strict criteria (less than 41 years old, at least 200 dives, no history of cardiovascular or decompression disease and other conditions such as multiple sclerosis or headache brain lesions. The randomization has been performed to exclude some population bias that can occur in such a voluntary-based selection process.

We tried to compare the fractal dimension of some clearly non-vascular spots in the white cerebral matter and the dimension of some other spots from other origins.

The purpose was to determine whether the "lesion-like" spots can be associated with the circulating arterial bubbles coming up to the brain from

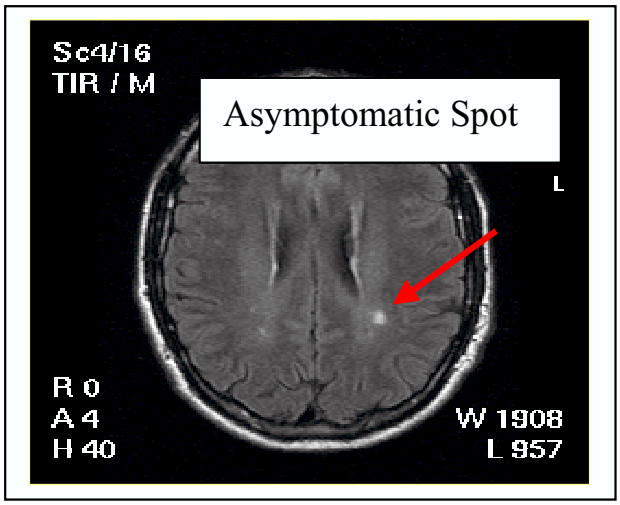

Fig. 3 Typical asymptomatic brain Spot In a diver.

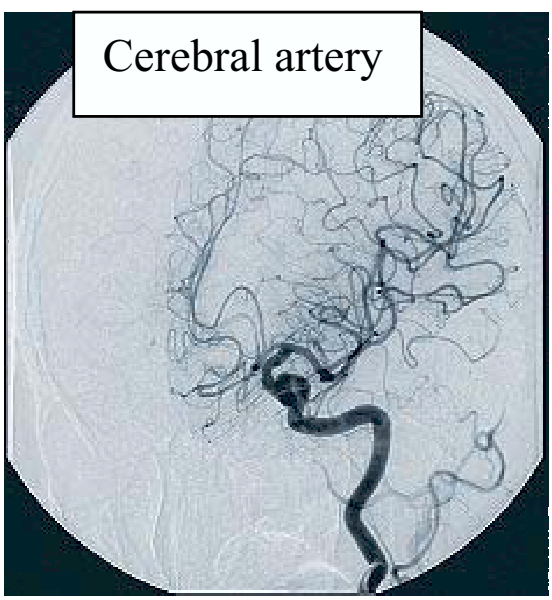

Fig. 4 Internal Carotid Angiography image.

the patent cardiac Foramen Ovale or just another unexplained or non-diving dependent mechanism.

Furthermore, to investigate the potential difference of the spatial distribution between the fractal dimension of ischemic lesions from cerebral vascular accident and the hemorrhagic ones, we separated them and controlled exclusively the clearly ischemic (thrombotic) ones.

If the "lesion-like asymptomatic spots" (see Fig. 3) were of vascular origin, their spatial distribution should be compatible either with the cerebral vascular images or the ischemic (thrombotic) lesion fractal dimension. In parallel, the fractal dimension of the internal carotid artery angiography (arteriography) was also compared to the others to investigate the compatibility with the cerebral vascular bed distribution (see Fig. 4).

4. RESULTS

We can find in our population of 42 asymptomatic divers (ramdomized out of 200, one excluded for multiple selerosis), four lesion-like white matter hyperintense spots. Then, we compare the fractal dimensions of 18 brain angiographies, nine images

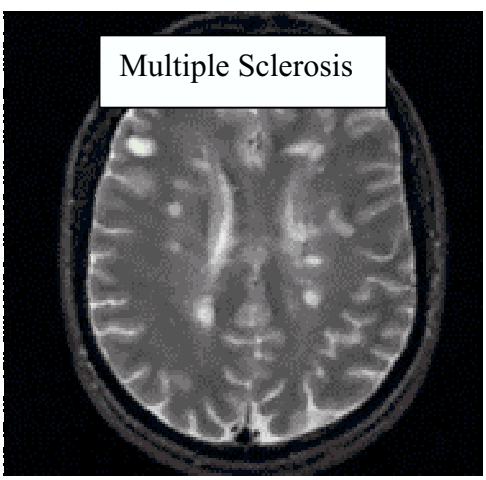

Fig. 5 Typical multiple sclerosis image in MRI.

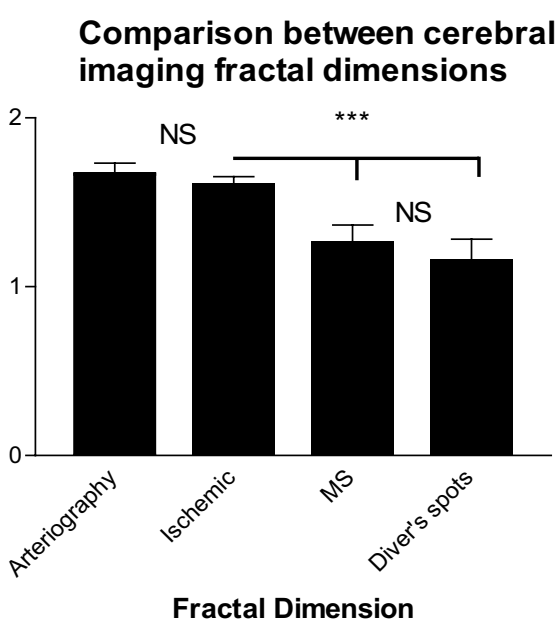

Fig. 6 Comparison between the respective fractal dimension obtained by means of the box counting method. $*** = p < 0.001$ according to anova with Neumans-Keuls discriminant post-test.

of multiple sclerosis, and five ischemic (thrombotic) vascular brain lesions images (see graph in Fig. 6).

The Anova statistical test was performed after testing the normality of the population and the Neuman-Keuls discriminant post-test was performed.

The differences between all the vascular dependent images fractal dimension and the "diver's spots" were highly significant ($p < 0.001$). Conversely, the differences between the vascular bed spatial distribution and the ischemic lesion images were not statistically different. This confirms that the fractal dimension is a good tool to use in this experimental paradigm.

The non-vascular brain lesion fractal dimension was not statistically different from the "diver's spots" one, thus our assumption was to postulate that those spots are not as clearly defined as the vascular-related ischemic lesions as generally admitted.

We furthermore looked at the proportion of patency of the Foramen Ovale in the tested population; we found a very large proportion: 63%; nevertheless the comparison between the number of spots found in the control population was not statistically different. This conforts us in our conclusions since the enormous proportion (usually the proportion is roughly 30%) should have given other alarming results if the "brain spots" were linked to the paradoxical embolization through the Foramen Ovale.

5. CONCLUSIONS

The fractal analysis of cerebral images is a good tool to determine whether the spatial distribution is compatible with the vascular bed and allows us to postulate another non-vascular mechanism. Moreover, the link between the patency of the Foramen Ovale of the heart and the diver's "brain spots" seems not to be as clear as previously postulated.[4,31]

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