

19. Brismar T, Collins VP, Kesselberg M. Thallium-201 uptake relates to membrane potential and potassium permeability in human glioma cells. *Brain Res* 1989;500:30-36.
20. Ruiz A, Ganz WI, Post MJ, et al. Use of thallium-201 brain SPECT to differentiate cerebral lymphoma from toxoplasma encephalitis in AIDS patients. *AJNR* 1994;15:1885-1894.
21. O'Malley JP, Ziessman HA, Kumar PN, Harkness BA, Tall JG, Pierce PF. Diagnosis of intracranial lymphoma in patients with AIDS: value of ²⁰¹Tl single-photon emission computed tomography. *AJR Am J Roentgenol* 1994;163:417-421.
22. Moustafa HM, Omar WM, Ezzat I, Ziada GA, El-Ghonimy EG. ²⁰¹Tl single-photon emission tomography in the evaluation of residual and recurrent astrocytoma. *Nucl Med Commun* 1994;15:140-143.
23. Yoshii Y, Satou M, Yamamoto T, et al. Experimental evaluation of the usefulness of thallium-201 single-photon emission tomography in the investigation and characterization of brain tumors in man and their response to treatment. *Eur J Nucl Med* 1993;20:39-45.
24. Suga K, Kume N, Orihashi N, et al. Difference in ²⁰¹Tl accumulation on single-photon emission computed tomography in benign and malignant thoracic lesions. *Nucl Med Commun* 1993;14:1071-1078.

Decompression Illness in Sports Divers Detected with Technetium-99m-HMPAO SPECT and Texture Analysis

Roger T. Staff, Howard G. Gemmell, Patricia M. Duff, Peter F. Sharp, Silvia E. Wilcock, Tom G. Shields and Francis W. Smith

University of Aberdeen, Department of Bio-Medical Physics and Bio-Engineering, Aberdeen Royal Hospitals; and Hyperbaric Research Unit, Robert Gordon University, Aberdeen, Scotland, United Kingdom

Diving for sport and recreation has increased in recent years, resulting in more incidences of diving illness. Therefore, we studied potential use of regional cerebral blood flow SPECT imaging with ^{99m}Tc-HMPAO in the management of divers who have experienced decompression illness (DCI). **Methods:** A group of ten sports divers who had no experience of DCI were compared with ten sports divers who had experienced at least one episode of DCI. Transaxial SPECT images were first compared objectively using a first-order texture measure and then subjectively using a receiver operator characteristic (ROC) experiment. Experienced observers were asked to rate images subjectively in terms of the images' textural appearance. **Results:** Both these techniques showed that there is a statistically significant difference between the two groups and the images produced by the DCI divers were generally more coarsely patchy when compared to the non DCI divers. The quantitative texture technique proved significantly better in identifying divers with DCI than the visual analysis by observers using ROC curves. **Conclusion:** Differences between the cerebral blood flow patterns of sports divers who have experienced DCI and sports divers who have no experience of DCI can be detected using ^{99m}Tc-HMPAO SPECT and a texture analysis technique.

Key Words: diving illness; SPECT; technetium-99m-HMPAO; receiver operator characteristics

J Nucl Med 1996; 37:1154-1158

With the popularity of diving for sport or recreation increasing in recent years, there have been more incidences of diving illness. The need for accurate and effective management of such patients is becoming increasingly important. The potential use of regional cerebral blood flow SPECT imaging with ^{99m}Tc-HMPAO in the management of divers who have experienced decompression illness (DCI) has been investigated by several groups (1-6). These investigations have produced conflicting results. For example, Wilmshurst et al. (2) found no evidence for or against the use of ^{99m}Tc-HMPAO SPECT in the management of DCI, whereas both Staff et al. (6) and Adkisson et

al. (3) found significant differences in image appearance between those who had experienced DCI and those who had not. Hodgson et al. (5), however, found the following: no difference between divers who had recently experienced DCI; divers who had experienced DCI some 3-5 yr earlier; control divers with no experience of DCI; and nondiving controls. The lack of correlation between the SPECT images and the clinical findings could be due to the ^{99m}Tc-HMPAO images being too sensitive for this diffuse disease (5). Adkisson et al. (3) also suggested that DCI should be recognized as diffuse and multifocal. The diffuse nature of DCI has also been identified by Calder (7) who, when considering the effects of DCI in terms of the histology, stated that "studies have shown definite evidence of damage to small cerebral vessels. The damage/change in the brain is diffuse, affecting both gray and white matter."

A popular assumption in decompression theory holds that DCI results from excess inert gas in the body which forms bubbles. After diving, insufficiently rapid washout of excess inert gases during ascent may form as a result of dive bubbles. Bubble growth can follow decompression when the pressure in the bubble reflects the pressure at greater depth and the ambient pressure has been reduced by decompression (8). This mechanism can result in symptoms and signs of DCI. The site and initial mechanism of bubble production within the body remains unclear. Gas bubbles may be intravascular, arising in either venous or arterial circulation, or extravascular, arising in situ within tissues. Intravascular and extravascular bubbles can disrupt tissue in a number of ways. They may exert a direct effect causing local mechanical damage and compression of the tissue. Additionally, intravascular bubbles may cause vessel occlusion with distal tissue ischaemia or disrupt the vascular endothelium. The bubbles may also cause secondary effects via activation of leucocytes, platelets and components of coagulation and complementary pathways (9).

With the exception of Staff et al. (6), the SPECT studies have attempted to analyze the images by detecting focal defects. Staff et al. (6) investigated the SPECT images in terms of the image texture and found significant differences between divers with DCI and a set of diving controls who had no experience of DCI.

Received Oct. 31, 1995; revision accepted Nov. 7, 1995.

For correspondence or reprints contact: Roger T. Staff, PhD, University of Aberdeen, Department of Bio-Medical Physics and Bio-Engineering, Foresterhill Aberdeen AB9 2ZD, Scotland, United Kingdom.

These results, however, showed that, although there was a difference between the groups investigated, the segmentation between the groups was not complete. Thus, a particular value of the texture measure did not necessarily allow a diagnosis of DCI to be made. It was suggested that matching groups that were more similar could provide more useful results and lead to better segmentation. One way to accomplish that is to limit the divers investigated to those divers who had not dived in a commercial environment. Commercial divers dive in a much wider range of conditions. For example, commercial divers generally dive deeper and experience higher hyperbaric pressures. They can dive on a range of mixed gas supplies such as oxygen and helium mixes and can dive in water of low temperatures. They can also undergo "bounce" dives where they rise to the surface immediately after a period at high pressure and then enter a dry chamber where they undergo recompression and slow decompression. Recreational divers generally do not experience these types of conditions. For this reason, it was decided to investigate groups of recreational divers only, thus eliminating the diversity which can occur in commercial diving.

Texture analysis has found a wide range of medical applications in a number of fields such as MRI and ultrasound. One of the simplest forms of texture analysis is based on first order statistics, such as gray scale moments (10). Other higher order and more complicated forms of texture analysis, such as the co-occurrence matrix, have also been found to be useful, such as in ultrasound imaging (11). While these higher order measures of texture are sensitive to more subtle variations in texture, such changes in texture may be difficult to detect in SPECT imaging due to the considerable amount of noise present. For this reason it was decided to limit our investigation to first order statistical measures of texture, such as mean gray level, which had been previously shown to be useful (6). The initial decision to investigate the value of texture analysis technique in examining ^{99m}Tc-HMPAO SPECT images of divers' brains was prompted by our clinical impression that such images were frequently coarsely patchy. It was therefore decided to test the ability of observers to identify divers who had experienced DCI by visual inspection of ^{99m}Tc-HMPAO transaxial images using ROC analysis. These results were then compared with the objective texture analysis method.

MATERIALS AND METHODS

Subjects

We studied two groups of sport or recreational divers. The first group contained ten sports divers who had experienced at least one episode of DCI. For these divers, DCI had been categorized using the original classification of decompression sickness (DCS) i.e., either Type I which took the form of, for example, musculoskeletal pain, skin rash, lymphatic symptoms and which appeared to have no neurological involvement; or Type II where symptoms were, for example, neurological, vestibular and cardiorespiratory. The DCI group studied in this investigation contained divers who had been classified as having experienced at least one episode of Type II DCS. Nine of the divers had only one episode of Type II DCS and one diver had experienced two episodes of Type II DCS. One of the divers who had experienced one episode of Type II DCS also had an episode of Type I DCS. The second group consisted of ten volunteer sports divers who had experienced no form of diving illness. A summary of the age and diving experience of each of these groups can be found in Table 1. The groups were not found to be significantly different using a Student's t-test.

TABLE 1
Summary of Subjects, Age and Diving Experience

	DCI divers	Control divers	t-test comparison
Mean age (yr)	32.1	29.9	t = 0.5
s.d.	11.9	7.1	p = 0.62
Range (yr)	20-53	23-44	
Mean number of yr diving	7.05	5.8	t = 0.74
s.d.	4.22	3.33	p = 0.47
Range (yr)	1.5-14	2-14	
Mean estimated number of dives	388.1	264.8	t = 0.59
s.d.	299.6	301.3	p = 0.56
Range	35-1144	17-1000	

Exclusion Criteria

The complete range of conditions that produces changes in ^{99m}Tc-HMPAO brain images is not known. In order to reduce the possibility of non-diving related factors influencing the results, subjects with a history of significant head trauma and/or prolonged anoxia or hypoxia were not included. None of the divers in this study had experienced a cerebral arterial gas embolism. None of the divers in this study had dived commercially. This study was carried out with the approval of the ethical committee of the University of Aberdeen, Scotland, UK.

Imaging Technique and Reconstruction

Divers were injected with 750 MBq ^{99m}Tc-HMPAO and imaged 15 min later on a rotating gamma camera fitted with a high-resolution collimator. The radius of rotation of the camera was kept as small as possible, however, in practice the range varied from 17 to 21 cm. The subjects were injected under the same conditions with their eyes open. The camera was interfaced to a MAPS 5050 data processor (Links Medical, Ltd., U.K.). The projection data was collected into 64 equally spaced image arrays each having dimensions of 64 × 64 pixels. Each projection image was acquired for 25 sec. Data was then corrected for nonuniformity and for the center of rotation variations, using a 40 million count flood. The data were then transferred to a Sun SPARCstation (Sun Microsystems, Inc., Mountain View, CA) and reconstructed using a filtered backprojection technique with a Hamming weighted ramp filter, using a Link Medical MAPS 10000 nuclear medicine software package. Transaxial sections were then re-oriented to lie parallel to the orbito-meatal line (reconstructed slice thickness was 6 mm).

Image Texture Assessment

The assessment of image texture in this work took two forms. The first form used a quantitative approach to textural assessment, the mean gray level measure of texture which is described below. The second form involved testing the ability of observers to identify visually textural differences between the two subject groups from the transaxial images.

The quantitative assessment of texture initially requires the definition of a surface or region of interest (ROI) in, or on, which the texture is to be assessed. In imaging modalities where the resolution is high, such as MRI, adequate regions can be defined simply by extracting a ROI within the boundaries of the organ of interest. Due to the poor resolution of the SPECT imaging technique and the nonhomogeneous blood flow pattern in the brain, no simple ROI or surface can be defined. The method used to overcome this problem was to radially sample the reconstructed images at the level of the gray matter.

Texture Surface

The technique for producing the texture surface has been previously described by Staff et al. (6) and is schematically

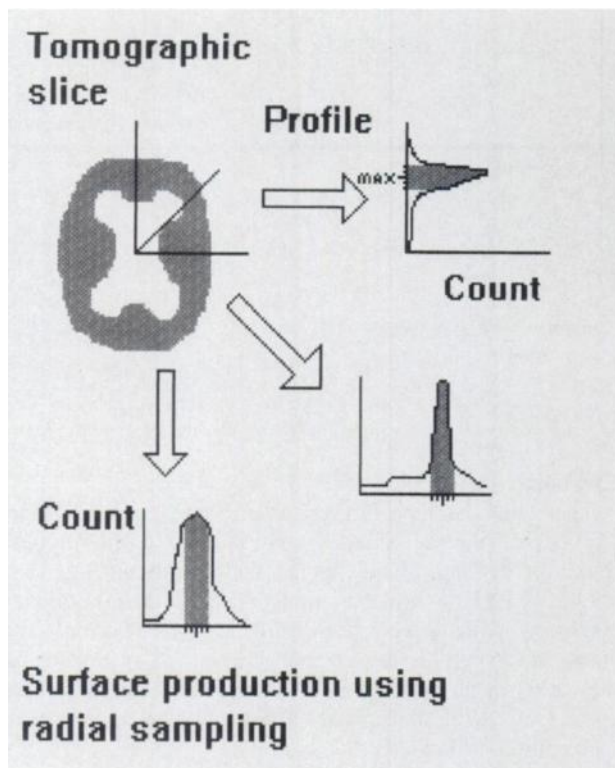


FIGURE 1. Schematic representation of the technique for producing the texture surface. Each profile represents the count density in a particular direction from the center of the brain to its edge. Sixty-four equally spaced radial profiles were calculated (three of which are shown). The shaded area under each profile represents the value of the surface pixel calculated by Equation 1.

represented by Figure 1. Using a reconstructed tomographic transaxial slice, the center of the brain in each slice was found first using a simple moment technique. The maximum pixel value (max) was then located along a line (L) from the center of the brain in direction n_θ terminating at the edge of the brain. The value of the texture surface (A) corresponding to this line and tomographic slice was then calculated by summing values of the two pixels either side of the maximum pixels with the maximum pixel value (Eq. 1).

$$A(s, n_\theta) = \sum_{\text{max}-2}^{\text{max}+2} L(y). \quad \text{Eq. 1}$$

This procedure was repeated for 64 lines equally spaced radially about the center, and for 6 slices in the gray matter in the brain above the level of the cerebellum. Due to the absence of an attenuation correction, the counts in the middle of the brain were low, meaning the maximum count of any radially sampled profile was always in the cortex. Therefore, regions in the middle of the brain, such as the basal ganglia, play no part in the formation of the texture surface. The technique of radial sampling is similar to the approach used by Ichise et al. (12), who described a method of two-dimensional mapping of cortical perfusion brain images by a cylindrical transformation of reconstructed SPECT data. Examples of the texture surface image can be seen in Figure 2. Each pixel within this image corresponds to a particular slice and direction n_θ . This procedure was automated with a computer program written from the image processing package PV Wave (Visual Numerics Inc., Boulder, CO). The sole task of the operator was to select the adjacent transaxial slices to be processed.

Quantitative Texture Analysis Technique

A gray level histogram (N) was produced by rebinning the surface image into 16 equally spaced histogram bins between the

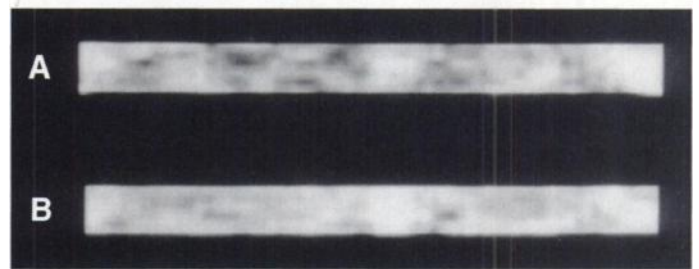


FIGURE 2. Typical surface image produced by a diver who experienced DCI (A). Typical surface image produced by a diver who had not experienced DCI (B).

maximum and minimum values of the surface image array. A probability histogram was then produced using Equation 2.

$$P(b) = \frac{N(b)}{N_T}, \quad \text{Eq. 2}$$

where N_T is the total number of pixels, $N(b)$ is the number of pixels with intensity b and $P(b)$ is the probability that a pixel has intensity b . The mean gray level of the probability histogram (m) was then calculated using Equation 3.

$$m = \sum_{b=0}^{B-1} bP(b), \quad \text{Eq. 3}$$

where B is the total number of histogram bins.

Observer Experiment

To discover if there is a visual textural difference between the images of each of the diving groups, the transaxial images of each of the divers were shown to four experienced observers. An example of these images can be seen in Figure 3. The images were presented to the observers using the color scale shown, which is the color scale used routinely at our institution and is one with which all the observers are familiar. The images were presented in the same random order to each observer who rated the images at one sitting. The observers were asked to rate the images on a scale of 1–6 depending on how patchy they thought the image texture appeared. A response of 6 represented the most patchy image and 1 the smoothest image. Due to the small number of images used in

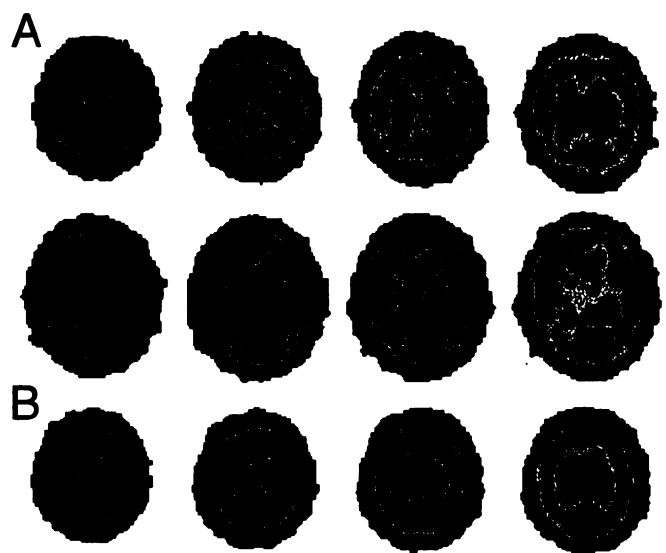


FIGURE 3. Typical sets of transaxial tomographic images shown to the observers in the ROC experiment. A set of images produced by a diver who has experienced DCI (A). A set of images produced by a diver who has no experience of DCI (B).

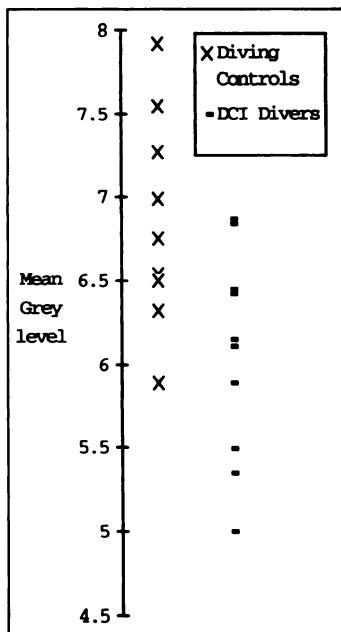


FIGURE 4. Mean gray level texture measure for each diver.

this experiment it was decided to pool the responses of the observers. The technique of pooling the data in this way is advocated by Swets and Pickett (13) when the observers are said to have similar skills, a condition which held in this study.

RESULTS

Quantitative Texture Measure

The distribution of the mean gray level texture measure for each of the groups can be seen in Figure 4. The average mean gray levels for the DCI and the control diving group were 6.06 (0.63) and 6.93 (0.64), respectively. The values in the brackets are the s.d. for each group. These results are statistically significantly different ($t = 3.07$, $p = 0.007$). Although this result shows a significant difference between the groups Figure 4 shows that there is overlap between the groups.

A technique for displaying the usefulness, i.e., the payoff between sensitivity and specificity, of using the mean gray level as a means of diagnosing the presence of DCI is to express the result as an ROC curve. The technique of producing a ROC curve from a texture measure has been previously carried out by Caligiuri et al. (14). To produce the ROC curve, six equally spaced thresholds of texture between the maximum and minimum values for the mean gray level found in this experiment were set. The values for the sensitivity (true-positive fraction) and specificity (false-positive fraction) for each diagnostic threshold were then calculated. These values and their fitted ROC curve can be seen in Figure 5. The ROC curve was fitted using software known as 'ROCFIT' which is based on the technique described by Dorfman and Alf (15). A commonly used figure of merit for assessing ROC curves is the area under the curve (16). The area under the ROC curve was 0.884 with a s.d. of 0.080.

Observer Experiment

The fitted ROC curve for the average observer and the experimentally recorded points, can be seen in Figure 5. As with the texture measure ROC curve, the line was fitted using 'ROCFIT.' The area under curve was 0.576 with a s.d. of 0.004. An observer who simply guessed would have an area under the ROC curve of 0.5. The area under the ROC curve for the combined observer is statistically different from that expected by pure chance ($Z = 19$, $p < 0.0001$) (16). Therefore, we can

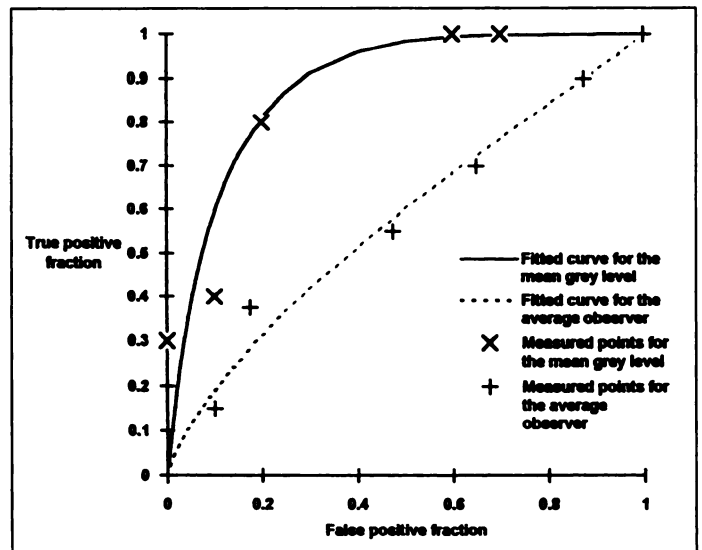


FIGURE 5. ROC curves for the mean gray level and the average observer.

say that while the average observer in this experiment performs poorly, this performance is significantly better than chance.

Comparison between Observer and Quantitative Experiment

A comparison between the texture ROC curve and the average observer ROC curve was performed using the software 'CORROC' (18) which was designed for the comparison of ROC curves from correlated data. The results show that the texture measure yields statistically significantly better discrimination between the groups than the observers' visual inspection ($\chi^2 = 12.13$, $p = 0.002$).

DISCUSSION

Recreational diving can have negative long-term consequences for health, particularly after DCI, as suggested in a recent study (19). Since there is no definite means of determining the presence of DCI other than the response of the patient to therapeutic recompression (2), a technique for the diagnosis and monitoring of DCS would be beneficial. Our work shows that it is difficult to diagnose the presence of DCI by visually assessing ^{99m}Tc -HMPAO transaxial images in terms of their image texture. The quantitative texture analysis technique, however, shows that it is possible to distinguish between a group of divers with DCI and a set of control divers. The approach described in this work requires minimal operator interaction and no observer interpretation.

The ability of the observers to identify from the images those divers who had experienced DCI was poor when compared to the texture measure approach. This could be attributed to the fact that the observers, although experienced, were not used to performing this type of task. The conventional way to analyze ^{99m}Tc -HMPAO images is to detect, locate and sometimes quantify focal defects (2). The assessment of overall image texture is a task with which observers are not generally familiar. The importance of training observers to perform specific tasks has been previously discussed by Metz et al. (17).

The full range of conditions that affects the appearance of the ^{99m}Tc -HMPAO image is not known. The lack of complete segmentation between these two groups may suggest that the image texture in this case is not simply determined by an episode of DCI. It may be postulated that the act of diving itself produces changes in the image texture.

Although, in this study, we have matched two groups in terms of the number of dives they have performed, this is no reason

for disregarding the number of dives as an influence on the image texture. In this study, the divers with the least diving experience in each of the groups produced the highest mean gray level texture measure (i.e., the smoothest image) in their respective groups. Our study focused on sports divers, where the type of diving the group undertakes can be completely different to dives undertaken by commercial divers, who may carry out both saturation and "bounce" dives using a variety of gas mixtures and forms of decompression. The effect of the number and type of dives on the image texture is a direction for further investigation.

CONCLUSION

In the past, investigators such as Palmer et al. (20), who studied the cerebral vasculopathy of divers, observed subtle and diffuse changes in the neuropathology. Their work concluded that "Type II DCI does not appear to lead to large areas of necrosis in the brain." This conclusion is consistent with our initial impression and findings in the present study: that in general divers who have experienced DCI have a coarsely patchy rCBF pattern.

Another direction for further investigation would be to use other forms of texture measure. The mean gray level texture measure used in this work is one of the simplest forms of texture analysis. First order texture measures such as the mean gray level can be affected by focal defects within the image. There is a potential problem with this approach. An alternative to the first-order measures would be to use more complex approaches such as a co-occurrence matrix (21) approach or the Fourier power spectrum approach (22). The techniques for texture measurement and classification are vast. The use of a more complex approach combined with a better understanding of the other factors that affect the appearance of HMPAO images may lead to improved segmentation between groups such as the ones investigated here.

REFERENCES

1. Macleod MA, Adkisson GH, Fox MJ, Pearson RR. Technetium-99m-HMPAO SPECT in diagnosis of cerebral barotrauma. *Br J Radiol* 1988;61:1106-1109.
2. Wilmshurst PT, O'Doherty MJ, Nunan TO. Cerebral perfusion deficits in divers with neurological decompression illness. *Nucl Med Commun* 1993;14:177.
3. Adkisson GH, Hodgson M, Smith F, et al. Cerebral perfusion deficits in dysbaric illness. *Lancet* 1989;July 15:119-122.
4. Evans SA. An investigation of the potential use of technetium-99-HMPAO-SPECT scanning in decompression illness. PhD thesis. The Robert Gordon University, Schoolhill, Aberdeen, Scotland; 1994.
5. Hodgson M, Smith DJ, Macleod MA, Houston AS, Francis TJR. Case control study of cerebral perfusion deficits in divers using ^{99m}Tc-hexamethylpropylene amine oxime. *Undersea Biomed Res* 1991;18:421-431.
6. Staff RT, Gemmell HG, Duff PM, Sharp PF, Wilcock SE, Shields TG, Smith FW. Texture analysis of divers brains using ^{99m}Tc-HMPAO SPECT. *Nucl Med Commun* 1995;16:438-442.
7. Calder I. Does diving damage your brain? *Occ Med* 1992;42:213-214.
8. Edmonds C, Lowry C, Pennefather J. In: *Diving and subaquatic medicine*, 3rd ed. Oxford: Butterworth-Heinemann Ltd; 1992:11-23.
9. Francis TJR, Gorman R. Pathogenesis of decompression disorders. In: Bennett PB, Elliot DH, eds. *The physiology and medicine of diving*, 4th ed. London: WB Saunders; 1982:454-480.
10. Gonzalez RC, Wintz P. Texture. *Digital image processing*, 2nd ed. Reading, MA: Addison Wesley; 1987:414-423.
11. Basset O, Sun Z, Mestas JL, Gimenez G. Texture analysis of ultrasound images of the prostate by means of co-occurrence matrices. *Ultrasonic Imaging* 1993;15:218-237.
12. Ichise M, Crisp S, Ganguli N, Tsui S, Gray BG. A method of two-dimensional mapping of cortical perfusion by cylindrical transformation of HMPAO-SPECT data. *Nucl Med Commun* 1995;16:386-394.
13. Swets JA, Pickett RM. *Evaluation of diagnostic systems: methods from signal detection theory*. New York: Academic Press; 1982.
14. Caligiuri P, Giger ML, Favus MJ, Hong J, Doi K, Dixon LB. Computerized radiographic analysis of osteoporosis: preliminary evaluation. *Radiology* 1993;186:471-474.
15. Dorfman DD, Alf E. Maximum likelihood estimation of parameters of signal detection theory and determination of confidence intervals—rating method data. *J Math Psychol* 1969;6:487-496.
16. Metz CE. ROC methodology in radiologic imaging. *Invest Radiol* 1986;21:720-733.
17. Metz CE. Statistical analysis of ROC data in evaluating diagnostic performance. In: Herbert D, Myers R, eds. *Multiple regression analysis: application in the health sciences*. New York: American Institute of Physics; 1976:365-384.
18. Metz CE, Wang P-L, Kronman HB. A new approach for testing the significance of differences between ROC curves measured from correlated data. In: Deconick F, ed. *Proceedings of Information Processing in Medical Imaging*. Hague, Netherlands: Nijhoff; 1984:432-445.
19. McQueen D, Kent G, Murrison A. Self-reported long-term effects of diving and decompression illness in recreational SCUBA divers. *Br J Sports Med* 1994;28:101-104.
20. Palmer AC, Calder IM, Yates PO. Cerebral vasculopathy in divers. *Neuropathol Appl Neurobiol* 1992;18:113-124.
21. Haralick RM. Statistical and structural approaches to texture. *Proc IEEE* 1973;67:786-804.
22. Weszka JS, Dyer CR, Rosenfeld A. A comparative study of texture measures for terrain classification. *IEEE Trans Syst Man Cybern* 1976;6:269-285.