

to metabolism. Since the approaches of Krivokapich et al. (4) and of Hutchins et al. (19) for measuring myocardial perfusion with ^{13}N -ammonia use kinetic data from the first several minutes after administration of tracers (contrary to what is used for "qualitative" imaging), these approaches also require tomographic units that are capable of faithfully recording the high count rates achieved (more difficult on tomographs with bismuth germanate detectors than on those with cesium fluoride detectors such as the scanner used in our study), and issues of randoms correction, deadtime, and spillover of radioactivity from blood to myocardium will be similar for ^{15}O -water as for ^{13}N -ammonia.

Finally, Dr. Buxton is concerned about the coefficient of variation in regional perfusion estimates made with ^{15}O -water. We believe these are largely due to the large regions of interest that we use for assessing perfusion. Smaller values have been published by Araujo et al. (15) and by Iida et al. (16) in results of their studies measuring regional myocardial perfusion in humans with PET and ^{15}O -water. We observe a coefficient of variation for ^{15}O -water similar to that for the extracted flow tracer, ^{62}Cu -PTSM (18). Although Dr. Buxton cites data regarding the coefficient of variation for studies with ^{13}N -ammonia, these data have not been published in the literature and we obviously cannot comment on personal communications.

In summary we believe that, at the present time, estimation of myocardial perfusion with ^{15}O -water is the most accurate and well-validated approach for measuring myocardial perfusion in experimental animals and human subjects. Although estimation of regional myocardial perfusion with ^{15}O -water is technically demanding and requires meticulous data collection and analysis as well as tomographs capable of faithfully recording high-count rates with high temporal resolution, we stand by the quantitative accuracy of the approach and believe that the conclusion drawn from our study, i.e., that older subjects exhibit a diminution in the hyperemic response to the standard dose of dipyridamole, is valid.

REFERENCES

1. Senneff MJ, Geltman EM, Bergmann SR. Noninvasive delineation of the effects of moderate aging on myocardial perfusion. *J Nucl Med* 1991;32:2037-2042.
2. Khouri EM, Gregg DE, Rayford CR. Effect of exercise on cardiac output, left coronary flow and myocardial metabolism in the unanesthetized dog. *Circ Res* 1965;17:427-437.
3. Holmberg S, Serzysko W, Varnauskas E. Coronary circulation during heavy exercise in control subjects and patients with coronary heart disease. *Acta Med Scand* 1971;190:465-480.
4. Krivokapich J, Smith GT, Huang S-C, et al. N-13-ammonia myocardial imaging at rest and with exercise in normal volunteers. *Circulation* 1989;80:1328-1337.
5. Ganz W, Tamura K, Marcus HS, Donoso R, Yoshida S, Swan JC. Measurement of coronary sinus blood flow by continuous thermodilution in man. *Circulation* 1971;44:181-195.
6. Nelson RR, Gobel FL, Jorgensen CR, Wang K, Wang Y, Taylor HL. Hemodynamic predictors of myocardial oxygen consumption during static and dynamic exercise. *Circulation* 1974;50:1179-1189.
7. Jorgensen CR, Kitamura K, Gobel FL, Taylor HL, Wang Y. Long-term precision of the N_2O method for coronary flow during heavy upright exercise. *J Appl Physiol* 1971;30:338-344.
8. Baller D, Schenk H, Strauer BE, Hellige G. Comparison of myocardial oxygen consumption indices in man. *Clin Cardiol* 1980;3:116-122.
9. Suga H, Hisano R, Hirata S, et al. Mechanism of higher oxygen consumption rate: pressure vs. volume-loaded heart. *Am J Physiol* 1982;242:H942-H948.
10. Hack SN, Eichling JO, Bergmann SR, Welch MJ, Sobel BE. External

quantification of myocardial perfusion by exponential infusion of positron-emitting radionuclides. *J Clin Invest* 1980;66:918-927.

11. Tripp MR, Meyer MW, Einzig S, Leonard JJ, Swayze CR, Fox IJ. Simultaneous regional myocardial blood flows by tritiated water and microspheres. *Am J Physiol: Heart Circ Physiol* 1977;232:H173-H190.
12. Bergmann SR, Fox KAA, Rand AL, et al. Quantification of regional myocardial blood flow in vivo with H_2^{15}O . *Circulation* 1984;70:724-733.
13. Bergmann SR, Herrero P, Markham J, Weinheimer CJ, Walsh MN. Noninvasive quantification of myocardial blood flow in human subjects with oxygen-15-labeled water and positron emission tomography. *J Am Coll Cardiol* 1989;14:639-652.
14. Huang SC, Schwaiger M, Carson RE, et al. Quantitative measurement of myocardial blood flow with oxygen-15 water and positron computed tomography: an assessment of potential and problems. *J Nucl Med* 1985;26:616-625.
15. Araujo LI, Lammertsma AA, Rhodes CG, et al. Noninvasive quantification of regional myocardial blood flow in coronary artery disease with oxygen-15-labeled carbon dioxide inhalation and positron emission tomography. *Circulation* 1991;83:875-885.
16. Iida H, Kanno I, Takahashi A, Miura S, et al. Measurement of absolute myocardial blood flow with H_2^{15}O and dynamic positron-emission tomography. *Circulation* 1988;78:104-115.
17. Shelton ME, Senneff MJ, Courtois M, et al. Concordant quantification of flow reserve by positron emission tomography and intracoronary doppler probes in patients with chest pain and angiographically normal coronary arteries [Abstract]. *J Nucl Med* 1992;33:836.
18. Bergmann SR, Herrero P, Anderson CJ, Welch MJ, Green MA. Measurement of regional myocardial perfusion in human subjects using copper-62-PTSM [Abstract]. *J Nucl Med* 1992;33:837.
19. Hutchins GD, Schwaiger M, Rosenspire KC, Krivokapich J, Schelbert H, Kuhl DE. Noninvasive quantification of regional blood flow in the human heart using N-13 ammonia and dynamic positron emission tomographic imaging. *J Am Coll Cardiol* 1990;1032-1042.

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Marrow Scintigraphic Changes After Hormonal Therapy

TO THE EDITOR: We have read with interest the paper of Berna et al. (1) in which they reported the marrow scintigraphic changes that they observed after hormonal therapy using $^{99\text{m}}\text{Tc}$ -antigranulocyte monoclonal antibody BW250/183 (AGMab) in two patients with bone metastases from prostate carcinoma. In this letter, we would like to report on our previously published experience with marrow scintigraphy in such patients ($n = 11$) using $^{99\text{m}}\text{Tc}$ -labeled nano-sized human serum albumin colloids in comparison to conventional bone scans using phosphonates (2,3).

In six patients, bone scans and marrow scintigraphy yielded identical findings (one status quo, two regressions, three progressions of disease). On the other hand, in five patients, marrow scintigraphy and bone scan findings diverged or disagreed. In these patients, and with regard to the ultimate evolution of the disease, marrow scintigraphy could be deemed superior to bone scans. Indeed, marrow scintigraphy showed clear progression of the metastatic process in two patients (who finally died of their cancers), whereas the bone scans remained unchanged. In two other patients, bone scans suggested disease regression but with unchanged underlying marrow scintigraphic lesions and with later

worsening of the disease. In the last patient, marrow scintigraphy suggested the complete healing of the medullary metastases despite a still pathological (although improved) bone scan but with later worsening of the disease. Our patients' results differ thus from those of Berna et al., except for our last patient. We do not wish to discuss yet again the differences between colloids, leukocytes or antibodies for imaging bone marrow (4,5), but we definitely conclude that in such patients with extensive or multifocal metastatic disease from prostate or breast carcinomas (data to be published), marrow scintigraphy using nano-sized colloids represents the simplest and least expensive way—not excluding its possible superiority to bone scanning—to evaluate these patients' responses to treatment.

REFERENCES

1. Berna L, Germa JR, Estorch M, Torres G, Blanco R, Carrio I. Bone marrow regeneration after hormonal therapy in patients with bone metastases from prostate carcinoma. *J Nucl Med* 1991;32:2295–2298.
2. Bourgeois P, Malarme M, Van Frank R, Wauters E, Ferremans W. Bone marrow scintigraphy and/or conventional bone scintigraphy for the diagnosis and management of skeletal metastasis from prostatic carcinomas [Abstract]. *Eur J Nucl Med* 1989;15:540.
3. Bourgeois P, Malarme M, Van Frank R, Wauters E, Ferremans W. Bone marrow scintigraphy in prostatic carcinomas. *Nucl Med Commun* 1991;12:34–45.
4. Bourgeois P, Fruhling J. Radioimmune imaging of bone marrow in patients [Letter]. *J Nucl Med* 1991;32:549–550.
5. Bourgeois P, Demonceau G, Stegen M, Ferremans W. Tc-99m-HMPAO-labelled leucocytes for bone marrow scintigraphy and evaluation of skeletal lesions: comparison to ^{99m}Tc-HSA colloid results. *Nucl Med Commun* 1991;12:621–627.

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The Localization of Indium-111-Leukocytes, Gallium-67-Polyclonal IgG and Other Radioactive Agents in Acute Focal Inflammatory Lesions

TO THE EDITOR: With great interest, we have read the results of the excellently designed animal study presented by McAfee et al. in a recent issue in which eight different radiotracers for localizing experimental abscesses in dogs were investigated and the local uptake ratio was calculated (1).

The final results of the study demonstrated the superior quality of ¹¹¹In-oxine-labeled granulocytes especially in comparison to the other investigated radiopharmaceuticals. A comparison with monoclonal mouse antibodies directed against the human granulocyte epitope NCA-95, labeled with ^{99m}Tc (Mab BW 250/183, Granulocyte[®], Behringwerke AG) or ¹²³I (Mab 47, Granuloszint[®], Mallinckrodt), was impossible due to species-specificity.

At our institutions, like in many others in Europe, ^{99m}Tc-labeled Mab BW 250/183 is frequently used for clinical applications concerning infection and inflammation. The simple in-vivo use, a ^{99m}Tc label, the logistic advantages and the lower radiation burden are important facts that emphasize this modality from a

clinical point of view. The sensitivity, specificity and accuracy are similar to the reported data from studies with ¹¹¹In-oxine granulocytes (2–9). Those studies include infections of the musculoskeletal system.

In regard to the limitation in transferring data from animal experiments to humans and the clinical results of anti-NCA-95, we cannot agree with the general conclusion of the authors that ¹¹¹In-granulocytes are superior to all other agents for localization of infectious lesions and that other options only play the part of a substitute. In our opinion, isolation and labeling procedures become more unpopular, because they are time-consuming procedures and there is the risk of infection from the AIDS virus.

Indium-111-oxine-labeled granulocytes have been the gold standard for many years, but the development of new monoclonals has become successful and seems to be as effective in clinical routine. An important future task will be to list the different available radiopharmaceuticals and to evaluate their various indications for localizing foci of infections.

REFERENCES

1. McAfee JG, Gagne G, Subramanian G, Schneider RF. The localization of indium-111-leukocytes, gallium-67-polyclonal IgG and other radioactive agents in acute focal inflammatory lesions. *J Nucl Med* 1991;32:2126–2131.
2. Becker W, Wolf F. Immunszintigraphie von Blutzellen. *Nucl Med* 1987;28:148–159.
3. Becker W, Borst U, Fischbach W, Pasurka B, Schäfer R, Börner W. Kinetic data of in-vivo labelled granulocytes in humans with a murine Tc-99m-labelled monoclonal antibody. *Eur J Nucl Med* 1989;15:361–366.
4. Joseph K, Höffken H, Bosslet K, Schorlemmer HU. In vivo labelling of granulocytes with Tc-99m anti-NCA monoclonal antibodies for imaging inflammation. *Eur J Nucl Med* 1988;14:367–373.
5. Locher JTH, Seybold K, Andres RY, Schubiger PA, Mach JP, Buchegger F. Imaging of inflammatory and infectious lesions after injection of radioiodinated monoclonal anti-granulocytes antibodies. *Nucl Med Commun* 1986;7:659–670.
6. Lind P, Langsteger W, Költringer P, Dimai HP, Passl R, Eber O. Immunoscintigraphy of inflammatory processes with a Tc-99m-labelled monoclonal antigranulocyte antibody (Mab BW 250/183). *J Nucl Med* 1990;31:417–423.
7. Sciuk J, Brandau W, Vollet B, et al. Comparison of technetium-99m polyclonal human immunoglobulin and technetium-99m monoclonal antibodies for imaging chronic osteomyelitis. *Eur J Nucl Med* 1991;18:401–407.
8. Reuland P, Winker KH, Heuchert TH, et al. Detection of infection in postoperative orthopedic patients with technetium-99m-labelled monoclonal antibodies against granulocytes. *J Nucl Med* 1991;12:2209–2214.
9. Segarra I, Roca M, Baliellas C, et al. Granulocyte-specific monoclonal antibody technetium-99m-BW 250/183 and In-111 oxine-labelled leukocyte scintigraphy in inflammatory bowel disease. *Eur J Nucl Med* 1991;18:715–719.

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REPLY: We thank Dr. Sciuk for his interest and kind remarks about our manuscript. Many of us in the U.S. have been following the interesting literature on the Behringwerke AG ^{99m}Tc-monoclonal antibody (Mab) BW 250/183 originally developed by Bosslet et al. (1). Although other anti-granulocyte Mabs are under development in Europe and in the U.S., none are available