Transverse-Sectional Imaging with Na\textsuperscript{18}F in Myocardial Infarction

S. Cochavi, G. M. Pohost, D. R. Elmaleh, and H. W. Strauss

Massachusetts General Hospital, Boston, Massachusetts

The potential utility of Na\textsuperscript{18}F for acute infarct imaging was assessed in a canine model with a positron camera. Transverse-section imaging of radiofluoride in five dogs with acute myocardial infarction, using a multicrystal positron camera, clearly demonstrated the zones of damage as areas of increased activity. The F-18 uptake in the infarct zones was found to peak at 48 to 72 hr after coronary ligation, as does Tc-99m pyrophosphate. Preliminary in vitro studies indicate that the relative F-18 uptake, 48 hr after ligation, is an inverse linear function of regional blood flow.


The possible use of Na\textsuperscript{18}F as an agent for the detection of acute myocardial infarction was originally suggested by Bonte et al. (1), who showed that relative uptake of F-18 in infarcted tissue was significantly lower than that of Tc-99m pyrophosphate (Tc-PYP). They therefore abandoned fluoride (F-18) in favor of Tc-PYP. Subsequent studies by Weber et al. (2) with longitudinal tomographic scanning also showed that F-18 uptake in acute infarction was insufficient for visualization.

The recent improvement in transverse-section tomography with positron cameras (3) has encouraged us to explore F-18 further as a tracer for imaging acute myocardial infarction. The tomographic reconstruction technique substantially improves contrast compared with that encountered in conventional two-dimensional display of three-dimensional regions. The prominent bone uptake of F-18 in the chest wall introduces significant background in the two-dimensional display, but this should be largely eliminated by transverse-section emission tomography.

To evaluate F-18 as an imaging agent for acute myocardial infarction, a series of experiments were performed using a multicrystal positron camera and a canine model of infarction.

**METHODS**

**Preparation of fluorine-18.** This is produced by the \textsuperscript{20}Ne(d,α)\textsuperscript{18}F reaction. Neon gas is added to a brass target box that has been passivated on the inside surfaces with fluorine. The neon is bombarded with a 6.5-MeV deuteron beam for 15–30 min at a beam current of 40 μA. Approximately 10–25 mCi of F-18 are prepared in this way. The radiofluoride solution is passed through a Millipore filter before administration.

**Positron imaging.** The multicrystal positron scintillation camera employed in the present study (4,5) has two opposing parallel planar detectors containing 140 NaI(Tl) crystals arranged in 12 rows 2.8 cm apart. Since each crystal pair has a sensitive area 1 cm in diameter (full width at half maximum), two-dimensional images are collected by moving these parallel crystal arrays through 25 different positions until the entire plane is scanned.

Tomographic images are obtained by rotating the camera through 15 equal angles of 11.25° and each crystal creates five internal angles with opposite crystals. Data from 75 equal angles are generated for tomographic reconstruction and a total of 23 tomographic planes are generated from the 12 rows of crystals and the 11

Received Oct. 30, 1979; revision accepted April 2, 1979.

For reprints contact: Gerald M. Pohost, Cardiac Unit, Massachusetts General Hospital, Boston, MA 02114.
intermediate planes. The field of view is 32 cm in length.

The data from the detectors are collected directly into a computer system and recorded on a magnetic disc.

Three-dimensional reconstruction algorithm. For the reconstruction of transverse sections, the images are taken at equally spaced angles around the object. The events in a transverse-sectional "cut" are then extracted from the multiple images and a filtered back-projected transverse-sectional reconstruction is performed. The reconstructed data are then displayed as an interpolated 128- by 128-element image with 64 gray levels for analysis. Planar images are used for identification of the transverse section of interest.

Production of radioammonia. Nitrogen-13 is produced in our laboratory by the $^{12}$C(d,n)$^{13}$N nuclear reaction according to Tilbury et al. (6). Methane gas is bombarded with a 6.5-MeV deuteron beam of $30$–$40$ $\mu$A for $10$–$15$ min. The product gas is trapped in $10$ ml of saline. About $25$ mCi of $^{13}$NH$_3$ is produced. Purity analysis is performed on GC and HPLC chromatograms.

Experimental myocardial infarction in dogs. Five mongrel dogs (19–22 kg) were anesthetized by i.v. injection of pentobarbital (30 mg/kg). A left thoracotomy was then performed under sterile conditions. Multiple (2–4) progressive ligations of confluent branches of the left anterior descending coronary artery were carried out until approximately 10–15% of the left ventricle (anterolateral or apical surface) appeared cyanotic. Transient ectopic ventricular activity was controlled by i.v. injection of 30 mg lidocaine. After the ligations were placed, the chest was closed and the animal allowed to recover. An i.v. injection of 1 g of sodium cephalothin was given to each animal to prevent infection.

F-18 and N-13 animal studies. In each of the five dogs studied, planar perfusion images were made initially with the relatively short-lived agent $^{13}$NH$_4$OH ($T_{1/2} = 10$ min). Doses of 4–6 mCi of radioammonia were injected i.v. and images collected 5 min later. Then, 4 mCi of Na$^{18}$F in saline were injected i.v. Approximately 1 hr after injection, planar F-18 images were made. In addition, F-18 left lateral images were taken on several occasions between 6 hr and 12 days after ligation. Transverse-section images were obtained as follows. First, transmission data were collected by placing a plane source of the positron-emitting radionuclide Ga-68 on the face of one detector head before any activity was injected, and 90 images were acquired as the camera was rotated 180$^\circ$ around the subject. Second, the plane source was taken out and the detector rotated to the initial position. Then, 4–6 mCi of $^{13}$NH$_4$OH were injected i.v. and data collection started 5 min after injection. The total collection time for the N-13 transverse-section study was 10 min. Left lateral N-13 images were collected for 5 min each. Third, carrier-free Na$^{18}$F in isotonic saline was injected i.v. The camera heads were set in the initial position and the collection of F-18 data for transverse-section study started 1 hr after injection. During this waiting period, the N-13 images were processed.

In vitro studies: Comparison of F-18 uptake with perfused Sc-46 microspheres. Two additional dogs were injected i.v. with 2 mCi of Na$^{18}$F 2 days after ligation. Two hours after injection, the thorax was reopened and 30 $\mu$Ci of 8- to 10-$\mu$m carbonized microspheres labeled with Sc-46 ($T_{1/2} = 84$ d) (7) were injected into the left atrium. Two minutes later, the animals were killed and 40 samples of about 1 g were taken from the occluded myocardial region and the nearby normal zones. The F-18 and Sc-46 activities of each sample were measured by gamma well counting. Corrections were made for physical decay of the F-18 and the activities were normalized to relative activity per gram. The uptake of the Sc-46 microspheres was used to determine the relative regional blood flow for each sample.

RESULTS

The first dog studied with F-18 demonstrated dramatic uptake in the infarcted zone at 24, 48, 72, and 96 hr after ligation. No uptake was found at 6 hr or 1 week after ligation. Figure 1 shows right lateral images of this dog taken with N-13 and with F-18, at 48 hr after ligation. The infarcted apical region is indicated by an arrow.

FIG. 1. Right lateral images of N-13 (left) and F-18 (right) taken with Dog 1 in same position. Upper images are same as lower ones, but made with different contrast. Animal was imaged 48 hr after occlusion. Infarcted area is clearly visible at apex in lower ammonia image. Increased focal activity shown on F-18 image is located at same region as decreased area, as can be seen in low-contrast images.

THE JOURNAL OF NUCLEAR MEDICINE
Note that the focal area of increased F-18 is located in the same region as the focal area of decreased N-13. A series of right lateral F-18 images was taken up to 12 days after infarction. The region of apical myocardial infarction was best defined on the F-18 images obtained at 48 and 72 hr after ligation. By 12 days, an F-18 area of increased activity was no longer evident. The second dog studied is shown in Figure 2. Left lateral images were taken at 8, 20, and 48 hr, and 7 days, after ligation. The intensity of F-18 uptake in the region of the infarct was much lower than that of the first dog but it also peaked at 48–72 hr. Three additional animals displayed F-18 increased activity in the region of infarction that were similar to those in the second dog studied. It was difficult to define myocardial uptake clearly in the left lateral planar images in the four later dogs because infarct activity was obscured by prominent bone activity. Figures 3 and 4 show transverse-section studies with N-13 and F-18, at 48 hr after ligation, from two representative dogs. The outline of the slice is as follows: the large bright region in the F-18 image (B) is the spine, and the infarcted area on the left side of the heart produces a well-defined N-13 decreased area of radioactivity (A) and an F-18 increased area (B) as indicated by arrows. A bright dot was used to mark this region on the computer display for comparison of N-13 and F-18 tomographic images.

Figure 5 shows six consecutive transverse-section F-18 images (out of the 23 available) of the initial study animal 24 hr after coronary ligation. The 1.4-cm tomographic cuts, which depict slices 1 cm thick, are obtained above the heart (A and B), through the heart (C, D, and E), and below the heart (F). The increased activity corresponding to the extent of infarction is defined in these three slices (arrows).

In vitro tissue studies demonstrated the relative distribution of F-18 compared with Sc-46 microspheres. In Fig. 6 the uptake of F-18 is plotted against relative blood
flow as indicated by the microspheres for each of the two canine studies. By F-18 uptake, the maximum infarct-to-normal ratio is six or seven to one in both animals, and occurs in the region of lowest flow. Highly significant linear correlations between F-18 uptake and relative blood flow are demonstrated in Fig. 6 (r = 0.84 and 0.94; p < 0.0001 in each instance).

**DISCUSSION**

In previous studies (1,2) with either a gamma camera or a longitudinal tomographic scanner, F-18 activity was not demonstrable in zones of acute myocardial infarction. The present study, employing a multicrystal positron camera, shows that transverse-section imaging of F-18, made 24 to 72 hr after coronary artery ligation and 1 hr after injection, demonstrates F-18 accumulation in regions of myocardial infarction. The explanation for the success of fluoride imaging in these studies is unclear, for previous studies revealed poor concentration of the tracer in the zone of infarction (1,2). Two reasons that should be considered are that small differences in radiopharmaceutical preparation could alter the distribution of tracer, or—less likely—that the transverse-section imaging improves resolution of F-18 distribution. The latter explanation seems unlikely because the planar images recorded with the positron camera (Figs. 1–3) also reveal the presence of the lesion. It is possible that differences in radiopharmaceutical, such as pH or the presence of carrier, could possibly play a role, but this unproven explanation requires further investigation. The present study does indicate that the optimum time for imaging occurs 48–72 hr after ligation, similar to that for Tc-99m pyrophosphate (8).

The preliminary in vitro studies show an inverse linear correlation between F-18 uptake and blood flow as determined by microspheres. These data suggest that direct quantification of F-18 activity using positron computed tomography might provide a means of measuring blood flow. This result is in contrast to those obtained with Tc-99m pyrophosphate and similar agents, which provide maximal concentration in regions with 30–40% of normal blood flow (7). In regions with lower or higher blood flow, there is progressively less pyrophosphate activity.

Fluorine-18 activity in the present study appears to be inversely related to blood flow, with the regions of
greatest uptake in the regions with lowest flow. Since we made no direct comparison between Tc-99m pyrophosphate and F-18 in the present study, the relationship between these cannot be stated. Suffice it to say that both agents are bone seeking, and their mechanism of uptake is most likely similar. Since the fluorine ion is small relative to Tc-99m pyrophosphate, it may diffuse more readily into regions of lower flow. Further comparisons are needed.

Infarct size may be quantitated using this transverse-section approach by planimetry of the area of F-18 uptake and multiplying by the 1.4-cm section thickness. Volumes from all sections with increased radioactivity can be summed to determine infarct size. Positron computed tomography has the advantage of allowing transverse-section tomographic reconstruction, and we anticipate a more accurate means of quantifying infarct size than is available with conventional single-photon imaging using agents such as Tc-99m pyrophosphate. An approach to quantification of infarct size has been reported by Willerson et al. from standard gammacamera images (9), and although the results are encouraging, this method depends on geometric assumptions about infarct configuration. Recently, several tomographic approaches using single-photon emission tomography have been reported. Keyes and coworkers, using a gamma camera rotated around the subject, have reported success with tomographic reconstruction of pyrophosphate distribution (10). In addition, Kirsh and coworkers have described a multiaperture collimator that is capable of producing tomographic images using a wide-field-of-view gamma camera (11). Decision as to the best method for clinical practice will require additional patient studies.

In summary, our study demonstrates the feasibility of transverse-section imaging of acute myocardial infarction with Na\(^{18}\)F and a multicrystal positron camera. This approach would allow quantification of infarct volumes without the technical difficulties that may be encountered with Tc-99m pyrophosphate and single-photon imaging. The F-18 uptake in infarcted zones is similar to pyrophosphate in that it peaks 48–72 hr after ligation. Preliminary in vitro studies indicate that the relative F-18 uptake at 48 hr after ligation is an inverse linear function of regional blood flow.

ACKNOWLEDGMENT

The authors acknowledge the assistance of Dr. Donald J. Hnatowich and Messrs. William Bucelewicz and Michael Kaczmarek for production of F-18. Drs. David Chesler and Norbert Pelc developed the reconstruction algorithm. Messrs. Steve Weise and Richard Moore provided technical assistance. We also thank Drs. Kenneth McKusick and Gordon Brownell for helpful suggestions. This work was supported in part by the following grants: Training Grant ST32CA 0976-04CT, and NIH Grants HL-17665 and HL-21751.

REFERENCES