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Tomoscintigraphic Assessment of Myocardial Metabolic Heterogenity

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I-123-ω-heptadecanoic acid (HDA) was evaluated for myocardial scanning in 59 healthy volunteers and 133 patients, using a 7-pinhole collimator. Early (uptake) and late (retention) images were compared visually. Regional HDA elimination was also followed semiquantitatively based on the calculation of a retention-over-uptake ratio, R(φ), derived from the maximal counts/pixel in 60 midventricular slice sectors. The healthy heart concentrated HDA homogeneously in all segments with no difference between early and late images. The minimal R(φ), taken as representative of that myocardium with the best function, was unchanged after maximal ergometer stress and with dipyramidole-induced hyperperfusion. A circumscribed decreased HDA uptake is the clear-cut criterion for an abnormal finding. HDA tomography of the myocardium had an 86% sensitivity for myocardial infarcts (MIs) up to 4 wk old, and 83% for myocardial scars (MSs). Comparing early and late tomograms, we find a cool-warm sequence more often with acute and subacute MIs. A cool-cool or a cold-cold sequence dominated with MSs. HDA tomoscintigraphy cannot replace Tl-201 for the evaluation of regional coronary reserve in coronary heart disease.

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Free fatty acids (FFA) provide more than 80% of the energy needs of the beating heart (*1*). Uptake and utilization of C-11-labeled FFA in the myocardium can be quantified (*2–5*), but, high costs and logistic problems with the positron scintigraphy limit the general use of these substances.

FFA labeled with radioiodine on the end (ω−) position show a biological behavior similar to that of their natural analogs (*6–9*). I-123-ω-heptadecanoic acid (HDA) has been the most completely studied and can be produced industrially and delivered to the users within one half-life. Its 159-keV photons are registered with high efficiency and good resolution by the Anger camera. In view of its 13-hr half-life, short-term repeat studies are possible, and the total body radiation exposure remains low—30 mrad/mCi against 70–250 mrad/mCi with Tl-201 (*10*).

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Several reports on scintigraphically clear-cut myocardial defects demonstrate the usefulness of HDA in routine clinical examinations (*9,11–19*).

With HDA, not only its uptake but its retention and elimination should be followed scintigraphically. This can be done with sequential scans. Regional differences in HDA myocardial concentration, moreover, are registered best tomographically. Techniques using a moving detector or a moving collimator prevent data collection in a continuous mode from all left-ventricular segments. The 7-pinhole collimator, on the other hand, is well suited to sequential tomoscintigraphy; data are acquired simultaneously and continuously from all points within the field of view. This technique is relatively inexpensive, presents analog images with high contrast, and is recommended for quantitative evaluations (*20*). Preliminary studies have proven its applicability in HDA examinations (*18,19,21,22*).

We have set up an examination protocol based on a model that is intentionally confined to descriptive terms and it has now been used unchanged over two years on

more than 200 patients and healthy persons. Using HDA primarily in patients with myocardial infarction (MI), sensitivity and specificity were soon found to be commendably high. Two main types of myocardial lesions with different functional behavior could be identified, corresponding to acute or subacute MIs and to scars, respectively.

MODEL

Due to its high extraction rate (*13*) I-123 HDA is taken up by the myocardium within a few passes. After oxidative degradation (*6,7,23*) and nonspecific deiodination (*10*), ionic I-123 and I-123-labeled catabolites are released at various rates into the blood again but are not reutilized. Myocardial uptake and elimination can be followed with two images. In a scintigram starting 5 min after injection ("early"), the myocardium is distinguishable from the heart blood pool. For a "late" image we chose 30 min after injection, since at this time retention is not yet masked by the increasing background.

These two images permit an evaluation of the I-123 distribution according to: (a) the HDA uptake (early image), (b) its retention (late image), and (c) the HDA elimination (comparison of late with early image). Theoretically, at least five behavior patterns are possible (Fig. 1), one normal (a) and four pathologic (b-e), as follows:

a) In healthy persons a homogeneous distribution is expected in both images, if HDA is eliminated with the same rate constant in all segments (Fig. 1a).

Heterogeneous activity distribution suggests myocardial disease. In the model a solitary abnormality is assumed (Fig. 1, b-e). Comparing early and late images, four types of myocardial lesions are conceivable:

b) The I-123 HDA elimination alone can be prolonged. This leads to locally increased retention in the late image (warm-hot).

c) Focal uptake can be decreased but not completely lacking. If tracer elimination in the lesion and its surroundings have the same velocity, late and early images will be alike (cool-cool).

d) Uptake in the lesion can be decreased but elimination prolonged, thus reducing the late contrast between defect and normal myocardium (cool-warm).

e) In lesions with no uptake, the elimination can not be observed (cold-cold).

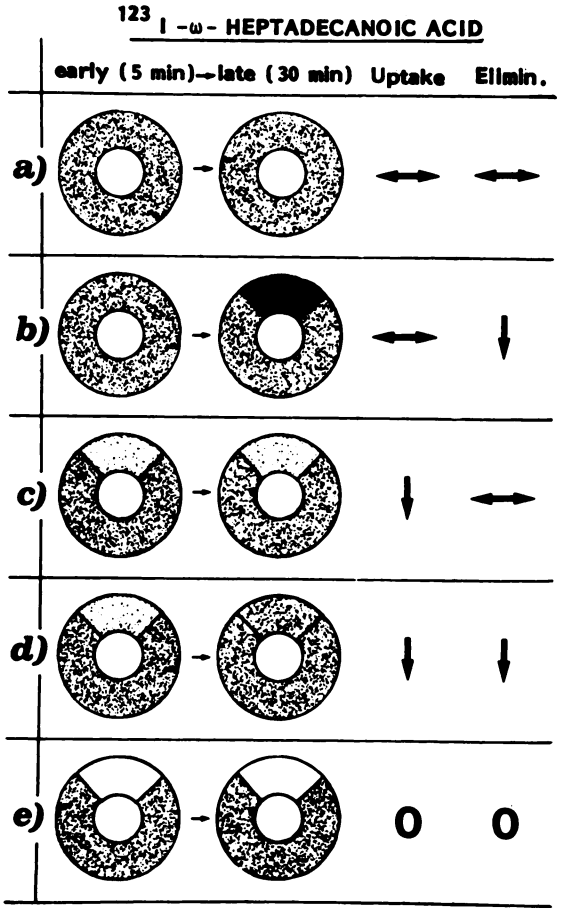

FIG. 1. Operational model for use of HDA in tomoscintigraphy. Schematic drawing of slices. An anterior unilocular lesion was assumed with the following different patterns: with normal (↔) or lower (↓) uptake, and with normal (↔) or retarded (↓) elimination.

TABLE 1. NORMAL RETENTION-OVER-UPTAKE RATIO, R(ϕ), AS A MEASURE OF MYOCARDIAL HDA ELIMINATION OF I-123 HDA

	n	Retention/uptake ratio* Min ± s.d.	Retention/uptake ratio* Max ± s.d.	Deceleration* Δ% ± s.d.
a_1. Normals, rest	25	0.641 ± 0.07	0.764 ± 0.09	26.7 ± 13.5
a_2. Normals, stress	17	0.588 ± 0.09	0.771 ± 0.1	31.87 ± 8.2
a_3. Normals, after dipyramidole	3	0.6 ± 0.1	0.783 ± 0.12	31.37 ± 10.7
a_4. Patients with normal results	38	0.628 ± 0.08	0.804 ± 0.1	29.03 ± 14.0
a. Normal findings, total	83	0.617 ± 0.08	0.786 ± 0.1	28.13 ± 12.0

* t-test: Not significant for all subgroups compared with a_1.

TABLE 2. I-123 HDA 7-PINHOLE TOMOGRAPHY: RESULTS

	n	Uptake defect +	Uptake defect −	R(ϕ)* minimum ± s.d.	Regional deceleration Δ% ± s.d.	Regional deceleration t-test
Normals, rest	25	0	25	0.614 ± 0.07	26.7 ± 13.5	
1. Myocard. infarct, 1st week						
Transmural	18	18	0	0.641+ ± 0.11	60.2 ± 44.4	<0.005
Subendocardial	6	6	0	0.528 ± 0.05	29.42 ± 18.7	NS
Suspicion	4	0	4	0.645 ± 0.08	32.05 ± 15.1	NS
2. Myocard. infarct, 2nd week						
Transmural	22	18	4	0.636 ± 0.08	46.9 ± 27.3	<0.005
Subendocardial	6	2	4	0.612 ± 0.07	28.73 ± 16.5	NS
Suspicion	3	0	3	0.66 ± 0.15	21.95 ± 13.7	NS
3. Myocard. infarct, 3rd week						
Transmural	12	11	1	0.588 ± 0.11	59.73 ± 38.6	<0.001
Subendocardial	2	2	0	0.65 ± 0.0	60 ± 0.0	<0.001
4. Myocard. infarct, 4th week						
Transmural	8	7	1	0.646 ± 0.04	38.14 ± 13.3	NS
Subendocardial	2	1	1	0.675 ± 0.04	24.95 ± 19.2	NS
5. Myocardial scar	30	25	5	0.641 ± 0.07	36.15 ± 19.4	NS
6. CHD, SIMI† +	9	2	7	0.637 ± 0.06	31.25 ± 14.5	NS
SIMI† −	7	1	6	0.623 ± 0.06	26.82 ± 10.5	NS
Suspicion	4	0	4	0.553 ± 0.18	37.44 ± 27.0	NS
7. Miscellaneous	4	4	0			

* t-test: Not significant (NS) for all groups and subgroups compared with the Normals.
† SIMI = Stress-induced myocardial ischemia.

An f-type lesion with low uptake and accelerated elimination (cool-cold) could be added to this series. Such lesions have been described by Van der Wall et al. (*9*) in the very early stages of MI.

PATIENTS, METHODS

From 1979 to the end of 1981, 250 persons were examined, after written or oral consent. We excluded 54 studies (randomly distributed) because of inadequate acquisition (n = 13), computer replay failure (n = 17), gastric masking of an inferolateral defect (n = 12), or liver activity over an inferoseptal lesion (n = 12). The patients, often in poor general condition, were not restricted regarding food or fat. Thirteen patients were examined twice. Thus, 209 complete HDA tomoscintigrams could be evaluated.

Twenty-five of 59 healthy volunteers (53 males, 6 females; mean age 38 ± s.d. 13.5 yr) had their tomoscintigraphy at rest, 17 after typical maximal ergometer stress, and 3 after dipyramidole infusion (*25*). (Table 1, a).

The 133 patients were examined at rest. Eighty-three had a history of acute to subacute MI (58 M, 25 F; mean age 58 ± 12½ yr). Intervals since onset of symptoms are shown in Table 2; 1-4. At least two out of three criteria—history and clinical evaluation, ECG, enzyme course—were required to assign a patient to one of the MI groups. Depending on the ECG followup, transmural and subendocardial infarctions could be differentiated. Because some patients came after a period of intensive care and because delivery of HDA was not warranted on a weekly basis, this grouping is based only on time since the MI, rather than on the clinical severity. The group with myocardial scarring (MS) (20 M, 10 F, mean age 60 ± 11 yr) contained 12 proven MS patients; we added eight who had MIs 5 wk earlier, and ten with still older MIs (Table 2:5). Excluded were scars from earlier MI's in patients who also had a current MI.

Another group of 20 ambulant patients with suspicion of coronary heart disease (CHD) (15 M, 5 F; mean age 50 ± 11.7 yr) was examined with a resting HDA study within one week after typical stress and redistribution thallium tomoscintigraphy (Table 2:6). Four patients with miscellaneous disease constitute the 7th group in Table 2.

Thirteen of the MI patients were re-examined 2 to 19 mo after infarction (*22*). They are listed twice, although with different results, in Table 2.

Seventeen patients with positive HDA lesions were

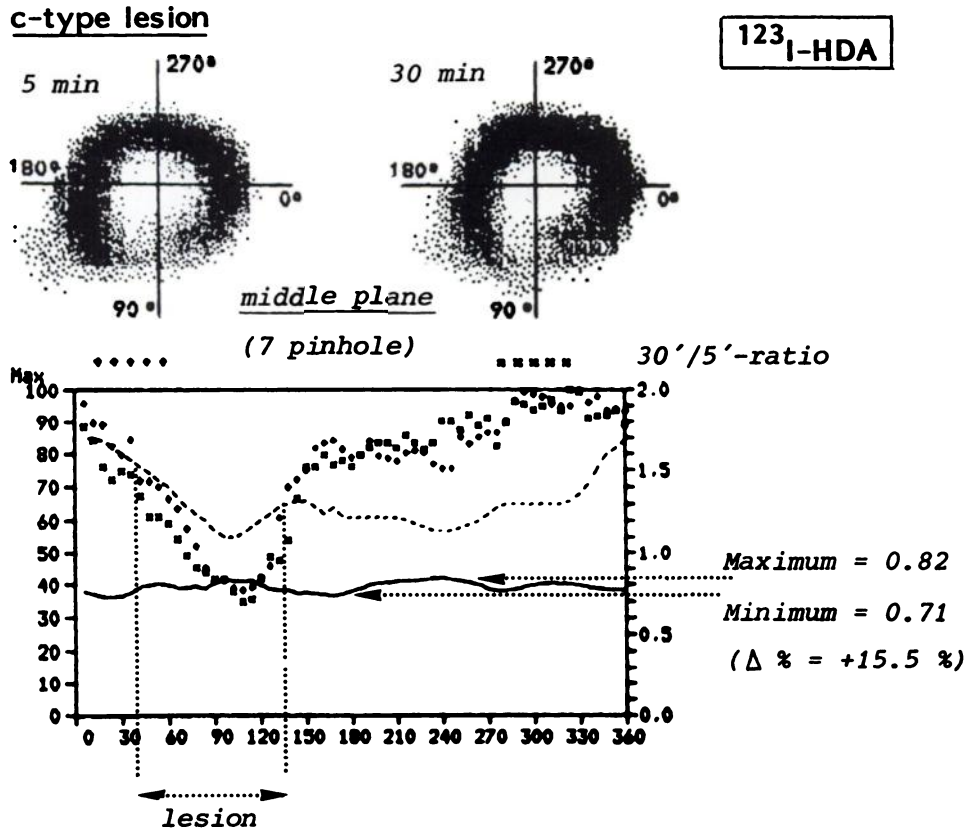

FIG. 2. C-type lesion with cool-cool sequence. "+" symbols for the circumferential measurements in early distribution, "x" for those of the late. The Vogel-Kirch −2 s.d. reference for normal Tl-201 results is shown as dashed line. The retention-over uptake-ratios, R(ϕ), are seen as a continuous line.

also examined with the first-pass radiocardiography. Akinetic and hypokinetic zones were evaluated on the basis of wall motion and trend pictures (*26,27*), independently and blindly by two of us (H.R. and G.M.).

I-123 HDA (3-4 mCi i.v.) was administered 10 minutes after 30 mg oral perchlorate to block uptake in stomach and thyroid. Correct placement of the 7-pinhole collimator and camera was ensured by persistence scope and Polaroid photos. Two 500,000-count images were made: the "early" starting 5 min after injection (~12 min acquisition time) and the "late" starting at 30 min (~18 min). Storage was in a dedicated computer. Display used a storage screen with 30% lower threshold, and a second scope for permanent records.

In Figs. 2-4, one middle slice from the early image is shown at upper left, the corresponding late image at upper right. Also shown is the crossing point of two orientating coordinates of the center of gravity for the circumferential measurements automatically calculated according to the "circle" program of Vogel and Kirch (*29,30*). We have modified this program, with an automated search of the maximum count per pixel between an inner and an outer ROI at each of 60 radii. These data are presented (normalized to 100%) in a graph in the lower part of the figure. The 0° to 360° profile for the early image is printed with "+" symbols, that for the late in "x" symbols. The dashed line is the −2 s.d. curve for the Tl-201 distribution in a normal group (*29*).

If the HDA uptake and elimination occur with similar time constants in all left-ventricular sections, then the activity profiles from both the early and late images imitate the dashed reference line but lie somewhat above it. A focal pathological process was assumed only when the patient's profile fell below this reference line for more than 30° (when steep) or 45° (when flat), and when a localized defect could be visualized in more than one slice (modified after: *31*).

As a further help we introduced the local retention-over-uptake ratio:

$$R(\phi) = \frac{c_2(\phi)/t_2}{c_1(\phi)/t_1}$$

where: ϕ = 0-360°, the angle designating some radius of interest, $c_1(\phi)$, $c_2(\phi)$ = maximal count densities found on radius ϕ in the early (c_1) and late (c_2) reconstructed images, t_1, t_2 = duration of the first frame (500 k) of the early (t_1) and late (t_2) acquisition periods.

The 60 values for R(ϕ) were then plotted as a continuous line after a 5 point-smoothing (seen as the solid line from 0°-360° in Figs. 2-4). This R(ϕ) is not influenced by the lower threshold used for the image presentation. De-

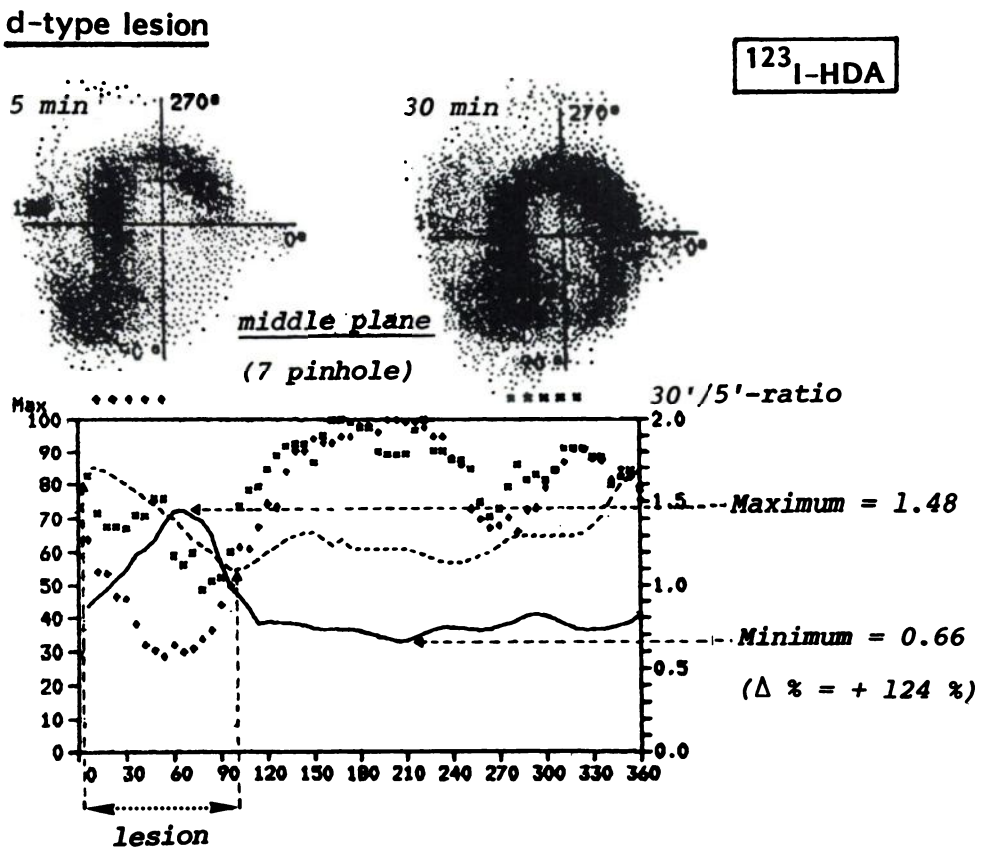

FIG. 3. D-type lesion with cool-warm sequence.

pendent on the HDA elimination velocity, the R(ϕ) values tend to be less than 1.

In contrast to the theoretical ideal behavior of R(ϕ) (constant over the entire left-ventricular circumference), even the curves from normal persons show slight fluctuations, the extent of which can be defined by the distance between minimum and maximum in the same curve.

The minima and maxima were separately averaged within the groups (Table 1 and 3) and compared by t-test for two grouped samples each, a $P > 0.005$ being judged as not significant (NS. in the tables). The distance between minima and maxima was calculated as deceleration Δ% in Tables 1-3 and Figs. 2-4. This value, which is independent of the absolute size of the minimum, was also statistically compared between the groups. All of these calculations were done only on one middle myocardial plane through the middle of the lesion.

Calculations for sensitivity, specificity, and predictive accuracy of a positive or negative test were based on positive and negative rates.

RESULTS

Normal compared with pathological findings. In normal persons the uptake and late retention of HDA is homogeneously distributed in the left-ventricular myocardium. The Tl-201 criteria for normal findings were fully met in early and late images in healthy subjects at rest (Table 1a_1) under stress (a_2), and after dipyramidole (a_3). Among the patients, 38 had normal findings (a_4): in them the minimal R(ϕ) could not be differentiated from the healthy ratio (Table 1).

Visually, only lesions of the c-, d-, and e-types could be found in the tomograms of patients. In the early images, c- and d-type lesions contained clearly less activity than the surrounding myocardium, but the myocardial ring was never completely interrupted in the area of the lesion (Figs. 2 and 3).

In c-type lesions (cool-cool) with identical findings in the early and late images (Fig. 2), the calculated minimum and maximum values were not significantly different from those of the normal group (Table 3). In fact, the coefficient of variation (V = s.d./mean) for the minimum values is practically the same as for a normal subject (0.15 against 0.16). Only the slightly higher V for the maximum values (0.17 relative to normal 0.10) is suspicious for a somewhat coarser inhomogeneity in the regional rates of release in c-type heart lesions.

Confirmation of a preliminary diagnosis. Twenty-four patients were examined during the first week after myocardial infarction, 18 with transmural and six with subendocardial extension of the lesion (Table 2:1). All of these patients showed clear-cut defects of HDA up-

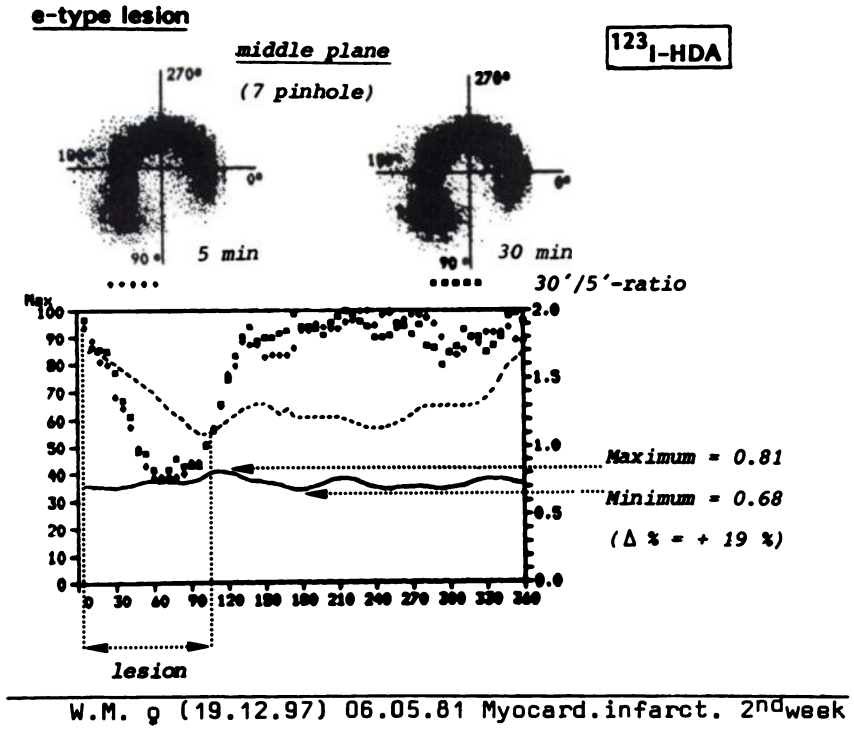

FIG. 4. E-type lesion with cold-cold sequence.

take in their tomoscintigrams, agreeing in location and size with ECG and enzyme findings. Four of the patients within this group were sent with clinical suspicion of MI, but this was ruled out by follow up. They had normal tomoscintigrams.

In those patients examined during the second week after MI, only 20 out of 28 infarcts could be confirmed (Table 2:2). False-negative results were more often found in patients with subendocardial (2/6) than with transmural MI (4/22). In three patients in whom the MI was suspected but not confirmed, the tomoscintigram was negative. Of the 14 patients seen 3 wk after their MIs, 13 were positive; the other patient had a 25° defect in only one tomographic slice, which was not considered diagnostic (*31*). Two other defects were missed among ten patients studied 4 wk after MI (Table 2:3-4).

Sensitivity, specificity and predictive accuracy of a positive or negative HDA tomoscintigram were compared for those 83 patients examined with proven and suspected infarction (Table 4).

TABLE 3. RETENTION-OVER-UPTAKE RATIOS, R(ϕ), AS A MEASURE FOR MYOCARDIAL ELIMINATION OF I-123 HDA (NORMALS VERSUS PATIENTS WITH LESIONS OF DIFFERENT TYPES)

	Retention/uptake ratio				Deceleration	
	Min ± s.d.	t-test	Max ± s.d.	t-test	Δ% ± s.d.	t-test
a. Normals n = 83	0.617 ± 0.08		0.786 ± 0.1		28.13 ± 12.0	
c. c-type lesions n = 32	0.634* ± 0.14	NS	0.806† ± 0.14	NS	27.38† ± 10.1	NS
d. d-type lesions n = 60	0.618* ± 0.09	NS	0.995‡ ± 0.19	<.001	61.56‡ ± 31.9	<.001
e. e-type lesions n = 5	0.656* ± 0.12	NS	0.83† ± 0.15	NS	27.14† ± 9.5	NS

* Normal myocardium outside the lesion.
† Center of the lesion.
‡ Peak over the lesion.
NS = Not significant.

TABLE 4. CLINICAL EVIDENCE OF MYOCARDIAL INFARCTION: CONFIRMATION WITH A I-123 HDA LESION

	1st–4th week	2nd–4th week
Sensitivity	86%	79%
Specificity	100% *	100% *
Predictive accuracy of a		
positive scintigram	100% *	100% *
negative scintigram	87%	83%

* No false-positive results with 25 normal volunteers and 4 suspected but not confirmed MIs.

TABLE 5. DISTRIBUTION OF d-TYPE LESIONS OVER A TOTAL OF 97 MYOCARDIAL HDA-UPTAKE DEFECTS

	n lesions	n d-type lesion
1. Myocardial infarct	65	46 (71%)
1st week	24	16 (67%)
2nd week	20	15 (75%)
3rd week	13	10 (77%)
4th week	8	5 (63%)
Transmural	54	39 (72%)
Subendocardial	11	7 (64%)
5. Myocardial scar	25	9 (36%)
6. CHD, SIMI = +	2	1
SIMI = −	1	1
7. Miscellaneous	4	3
Total	97	60 (62%)

Myocardial scars (Table 2:5) were delineated with regional defects of HDA in 25 of 30 patients (sensitivity = 83%).

Twenty patients suspected of having CHD were examined with both Tl-201 and HDA scintigraphy. In four patients the CHD could not be substantiated (negative stress ECG and normal coronary arteriograms); they gave normal HDA results. In two of nine patients with Tl-201-proven stress-induced myocardial ischemia (SIMI) (Table 2:6), the defects of HDA uptake were concordant; the other seven were normal (*Fig. 5*). In six of seven patients with negative Tl-201 findings, the HDA study was also normal; however, a defect was found in the remaining patient (with d-type behavior). (This patient was re-examined with Tl-201 two months later and was then found to have an unequivocal scar.)

The last group of four patients (Table 2:7), each with more than one HDA lesion, includes patients with terminal heart failure and one with cardiac sarcoidosis.

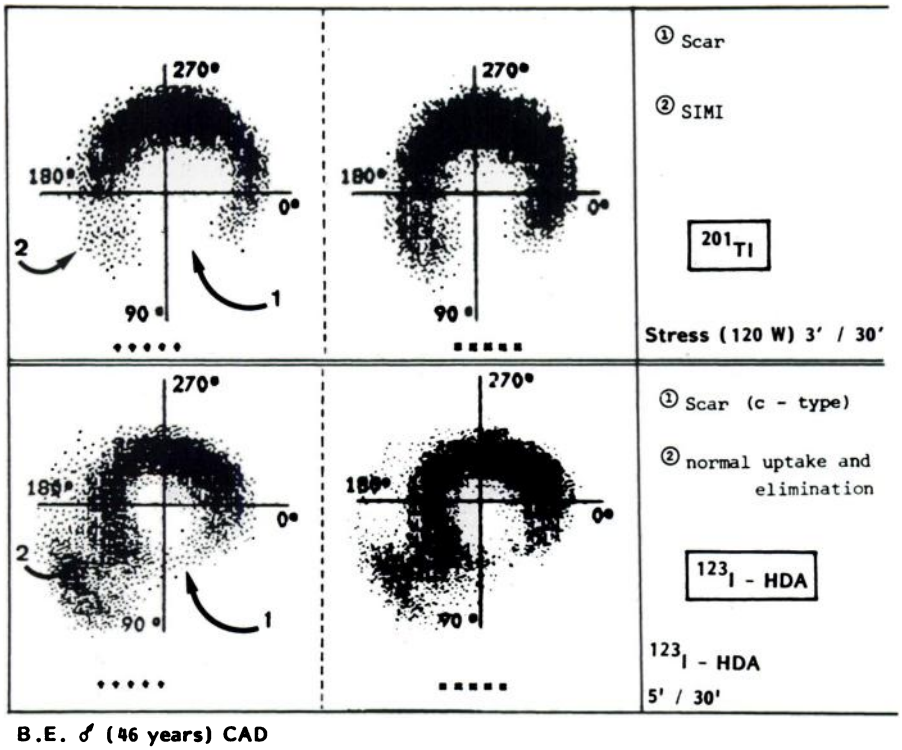

FIG. 5. Man, 46 yr old, examined with Tl-201 7-pinhole tomography and a typical stress protocol (upper pair): 1-scar after myocardial infarction several years previously, and 2-stress-induced ischemia (SIMI) in neighboring septal region. Same patient with HDA tomoscintigraphy at rest (lower pair): scar (1) confirmed by a c-type lesion. Normal uptake and retention of HDA by ischemic myocardium (2).

TABLE 6. MYOCARDIAL HDA-UPTAKE DEFECTS: A d-TYPE LESION AS AN INDEX FOR A 1st–4th WEEK MYOCARDIAL INFARCT

Sensitivity	71%*
Specificity	56%†
Predictive accuracy of a	
positive test	62%†
negative test	66%†

* True-positive rate = 46/65.

† True-negative rate = 18/32 (25 scars + 3 CHD + 4 misc.).

Typing of HDA lesions. There was a total of 97 uptake lesions. Of these, 60 (62%) were classified as d-type lesions, and 37 (38%) as c-type (cool-cool) or e-type (cold-cold). The incidence of d-type lesions was higher in patients with recent myocardial infarction than in those with scars (71% compared with 36%, Table 5). In number of patients with MIs followed through 4 wk, the d-type lesion was seen most often in the second and third weeks.

Is a d-type lesion a hint of an acute to subacute myocardial infarction? The true-positive rate is 71%, but this fairly good sensitivity is counterbalanced by worse rates for specificity and predictive accuracy (Table 6).

In 13 randomly chosen patients, follow up studies (average at 15 mo, range 2–19 mo after the first examination), demonstrated identical c- or e-type lesions of the same size in five out of ten. One very small lesion could not be confirmed. Four lesions converted to cool-warm behavior (Fig. 6: Note the cool-warm sequence along the borders between the defect and the normal myocardium in the very early tomograms). Two of these four had increased in size, and only the adjacent new defect zone followed the d-type pattern (Fig. 7).

Two initially cool-warm lesions kept their d-type behavior while increasing in size. One other converted to a smaller c-type lesion.

The size of an akinetic or hypokinetic zone, as visualized by first-pass radiocardiography, appeared to be unequivocally larger than the corresponding HDA myocardial lesion in three of nine patients with c- and e-type lesions; none was smaller. In contrast, three of the eight d-type lesions caused smaller zones of akinesia or hypokinesia, but never larger ones (Fig. 8, Table 7).

DISCUSSION

Our model for routine tomoscintigraphy was based primarily on the hypothesis that HDA uptake monitors myocardial perfusion and viability, and that HDA elimination rates reflect the over-all oxidative energy production by the myocardium (*7*). However, with such a simplified model, certain limitations must be carefully considered.

In the healthy myocardium the slope of the time-activity curve for free fatty acid (FFA) is not significantly affected by flow (*32*). Increased perfusion via exercise or dipyramidole does not enhance HDA uptake or accelerate HDA elimination in healthy subjects (*17*). Coronary reserve, therefore, is outside the province of HDA scintigraphy. Moreover, the Tl-201 stress-and-redistribution protocol cannot be applied, since HDA is broken down immediately and its catabolites have no affinity for the myocyte.

In the ischemic myocardium, uptake and elimination of HDA do not truly reflect its total oxidative metabolism. First, in this situation oxidative and anaerobic

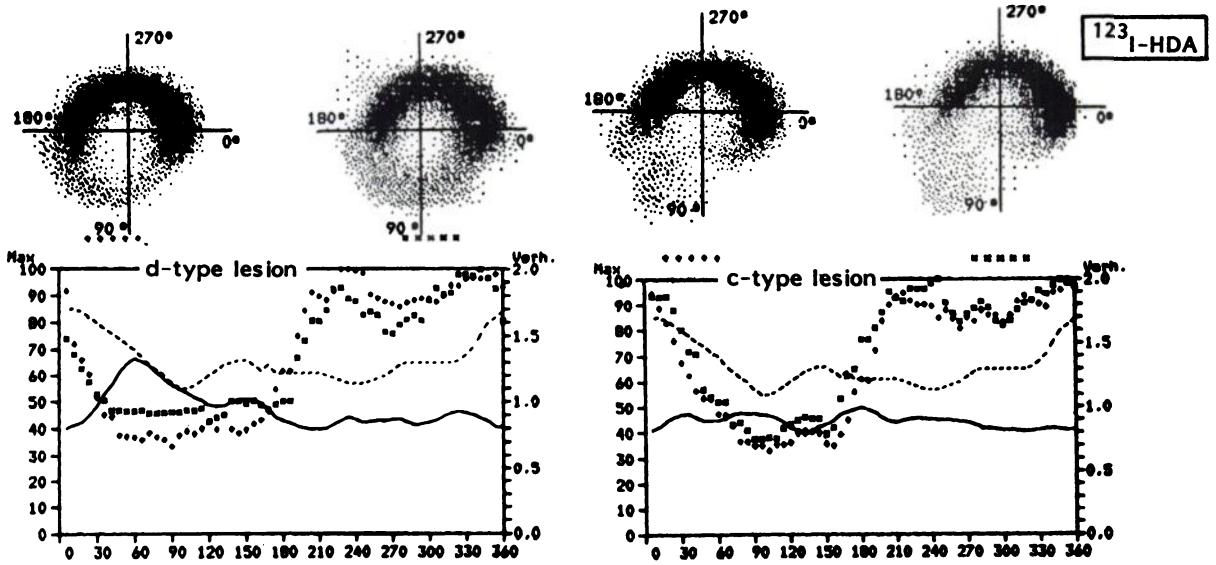

FIG. 6. MI, 1st week, with predominantly c-type lesion. On both borders with normal myocardium there is fainty d-type deceleration of HDA elimination (left side); 3 mo later (right side) there is d-type behavior throughout lesion.

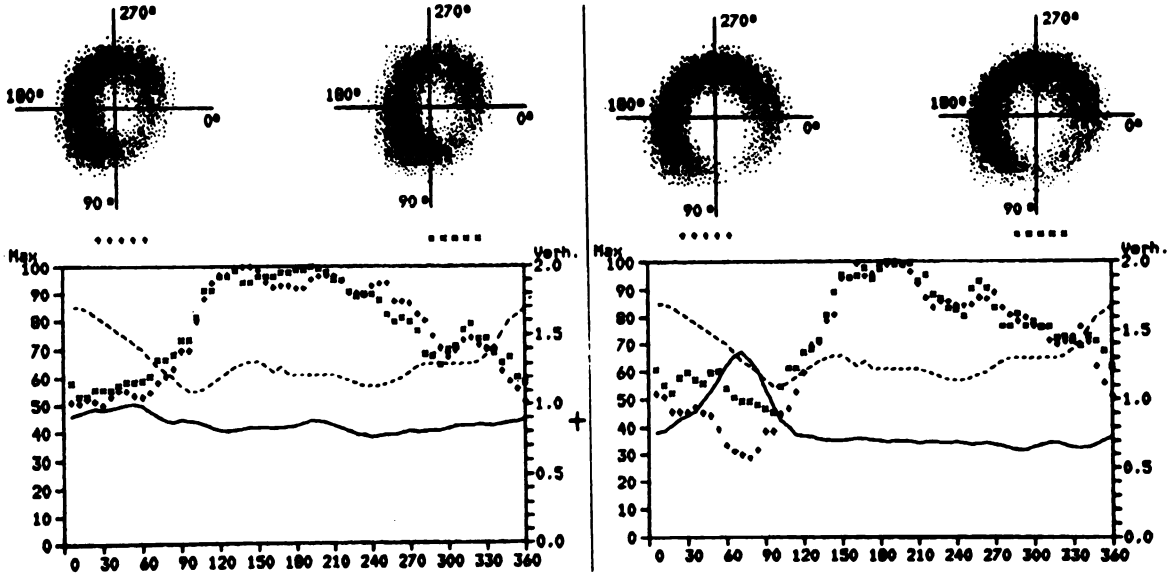

FIG. 7. A 2-wk-old MI with inferolateral myocardial defect (320°–70°) with c-type behavior (left side); 18 mo later defect has extended into inferior septum (70°–110°). This area follows a d-type sequence.

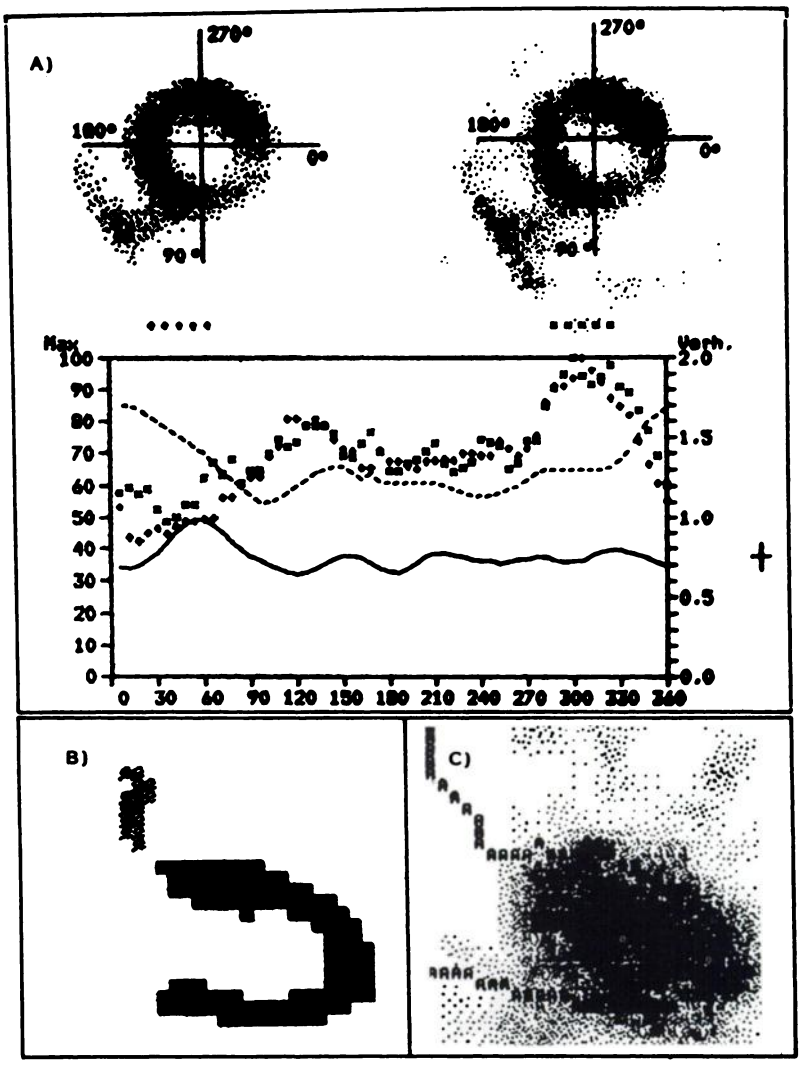

FIG. 8. Inferolateral d-type lesion (A) with a corresponding RAO first-pass wall-motion radiocardiogram (B) and parametric trend scintigram (C) of systolic emptying phase, neither of which shows any abnormalities.

TABLE 7. AKINETIC OR HYPOKINETIC ZONES (REGIONAL WALL MOTION BY FIRST-PASS RADIOCARDIOGRAPHY) COMPARED WITH THE CORRESPONDING HDA DEFECT

	Larger	Equal	Smaller	(n)
Type of HDA defect:				
c-/e-type	3	6	0	(9)
d-type	0	5	3	(8)

glycolysis are relatively and absolutely increased but remain unassessable with HDA examinations. Second, residual blood flow removes HDA catabolites more slowly from ischemic areas than from normal myocardium (*32*). Thus, elimination rates are biased by impaired myocardial blood flow. Third, the synthesis of neutral lipids is increased in ischemia (*33*). A relatively large amount of HDA might go this roundabout way, masking the diminished uptake of exogenous fatty acids and retarding their removal. In vitro findings, on the other hand, show that the incorporation of FFA into neutral lipids never plays a dominate role (*3*).

Even for an appraisal of true HDA oxidation rates, every clinical protocol is lacking in one critical point: the first turnover component, with a half-time between 1.7 min (*10*) and 2.8 min (*32*), which represents the immediate oxidation of two thirds of the extracted FFA, cannot be followed because of technical limitations. Scintigraphically observed elimination rates are derived mainly from a slower turnover pool that reflects esterification of one third of the FFAs to triglycerides, diglycerides, and phospholipids, all of which are temporarily deposited in the myocyte before being hydrolyzed and oxidized (*32*). Theoretically, the size and turnover of this slow pool should provide only supplementary information on the metabolic state of the heart. Practically, however, this slower pool—monitored by serial scintigraphic study—is the main, if not the only, source of information available on HDA metabolism. With our procedure, in fact, data acquisition could not be started earlier than 5 min after injection; moreover, only two measurements, each with rather long acquisition times, must serve as the references for the ratio calculation. As an illustration: Hoeflin et al. have published calculations that compare retention-over-uptake ratios with half-time values derived from simultaneously measured planar images (*18*). Based on their regression equation, the minimum $R(\phi)$ for normal persons of 0.6168 ± 0.098 (Table 1) corresponds to a half-time ranging between 13.0 and 36.7 min. For the maximum in normal subjects the average half-time is much higher (= 53.6 min). We also had to dispense with background corrections because of technical limitations.

Finally, there is the controversy as to whether or not C-11 fatty acids and ω-labeled FFAs have identical functional behavior (*6,10,23,24*). This needs further detailed evaluation. Based on our results, however, certain statements can be made:

1. The healthy heart takes up HDA homogeneously in all segments. This distribution, as seen in the early HDA images, parallels that of Tl-201, and HDA therefore falls within the limits given by Vogel and Kirch for Tl-201 (*29*).

Thus, the proven, continuous circumferential registration of uptake in the 7-pinhole tomographic slices is also valid for these early images with I-123 HDA. Late images show the retention of HDA—not the redistribution as observed with Tl-201—and are transitional stages of HDA elimination. The elimination observed between the early and the late images occurs in normal persons with the same velocity in all left-ventricular sections, so density remains homogeneous in the late images.

2. As far as can be seen in the early images, the uptake is not increased with increased energy needs, as after physical exercise (group a_2, Table 1) or with hyperperfusion due to dipyramidole (a_3). In addition, the elimination from healthy myocardium is not thereby increased, even adjacent to acute or chronic lesions. It follows that the routine determination of the elimination rates from scintigraphically normal myocardium would not result in relevant information, even with better techniques and shorter acquisition times.

3. The abnormal finding has one clear criterion: the circumscribed decreased HDA uptake. Warm-hot lesions with normal uptake but prolonged elimination (*14*), were never seen. Within those lesions with decreased HDA uptake, two behavior types can be clearly distinguished: those without HDA trapping, such as the c- and e-type lesions, and the d-type lesion with prolonged HDA elimination.

The differentiation between c- and e-type lesions can be made only by visual comparison of the tomographic sections recorded with a constant lower threshold, and has no quantitative support. However, as "combined c- or e-type lesions" these findings are a clear entity in contrast to the d-type.

Without a doubt the d-type defect takes up but cannot utilize HDA and/or has a prolonged release of HDA into the blood pool [mean $R(\phi)$ 1.0]. The quantitative evaluation is helpful in these patients, since small differences in density are frequently difficult to recognize visually in the scintigram.

4. HDA tomography of the myocardium is a method with high sensitivity and good specificity in patients with acute myocardial infarction. As concerns their ability to confirm or rule out MI, our results compare best with those seen using Tl-201 (*34,35*). A fall in sensitivity between the first and the subsequent weeks is also seen

with thallium-201: smaller lesions are delineated best immediately after the onset of the ischemic destruction but can be obscured later in the healing processes.

5. In a strict sense, one early distribution study should be sufficient to verify these results. But by comparing the early uptake pattern with the late distribution, one can separate lesions with constant cool or cold findings from those with a cool-warm pattern.

Are these different types merely artifacts? It is only an assumption that minimal HDA uptake in c- and d-type lesions occurs in residues of normal myocardium that survive amidst the necrosis in c-type lesions, or that the d-type lesion is caused by an increased esterification of HDA into lipids that have been accumulated in the necrosis (*33*). Our protocol cannot give accurate data to prove or disprove. We observe, however, that in some instances the akinetic or hypokinetic zone was smaller than the HDA d-type lesion, in contrast to c- and e-type lesion (Table 7). Cool-warm lesions do not cause wall-motion abnormalities to as great an extent as cool-cool or cold-cold lesions.

6. Thus, keeping in mind the fact that the incidence of d-type lesions is lower with scars than with acute infarction, one might reason thus: d-type lesions are dominated by necrosis, with residual viability in which fatty degeneration takes place and/or venous outflow is slowed but not obstructed. Scarring, as the late stage of healing, is not yet complete.

Such lesions with "prolonged clearance" (*12*), with "prolonged turnover rates" (*17,37*) or "prolonged anabolic tracer release" (*8*), or with a "delayed downslope", (*36*) have been interpreted as "ischemic areas" in patients with subacute MIs (*12,36*) and in those with CHD after exercise (*37*).

7. These observations lead to prognostic implications that may have therapeutic impact. Myocardial lesions with residual uptake but prolonged HDA catabolism are suspected of being unstable, and, since some coronary flow persists, should be able to react to protective or other therapeutic measures better than lesions without any residual HDA metabolism.

8. Although we did not find analogous lesions with Tl-201, we feel that further studies are needed to clarify whether or not HDA d-type lesions compare with those Tl-201 defects found at rest with a spontaneous late fill-in when serially scanned over 8 hr (*38*). On the other hand, transitional ischemia due to impaired coronary reserve will remain the domain of Tl-201 and the well-known stress protocols.

In the material presented here, 13% of the studies were lost to evaluation through computer and positioning failures. A further 6% with interference from stomach activity should have been avoidable. The 6% with masking of an infero-septal lesion by activity in the liver were quantitatively useless, but recognition or exclusion of a lesion was still possible.

Our typing is a rather coarse one. Follow-up studies, which should consider even smaller changes in regional Δ% values as well as small alterations in the lesion's size, will give more detailed information on the natural course of an individual MI and its response to treatment. Further advances could be accomplished with a mobile 7-pinhole camera.

FOOTNOTE

* I-123 ω-heptadecanoic acid: EIR, Würenlingen CH, (p,5n) reaction: at calibration time I-125 impurity $\cong$ 1%, no I-124 impurity.

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