RADIOCHEMISTRY AND RADIOPHARMACEUTICALS

Radioiodinated Fatty Acids for Myocardial Imaging: Effects of Chain Length

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Terminally iodinated long-chain fatty acids have been used experimentally and clinically as myocardial imaging agents. Six ω-iodo fatty acids ($I(CH_2)_nCO_2H$, where n = 10, 12, 15, 18, 21, 26) have been synthesized and tested in rats. Myocardial extraction values and heart-to-blood ratios are affected by chain length. Extraction is shown to be highest for n = 18 and 21, as are heart-to-blood ratios at 5 min. The cellular fate of the fatty acid changes from that of β-oxidation for n ≤ 15 to predominantly triglyceride storage for n = 18 and 21, as shown by analysis of rat heart homogenates by thin layer chromatography at two time intervals.

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Gamma-emitting tracers, such as thallium-201, have been used experimentally and clinically to detect abnormalities in regional myocardial perfusion. Another promising class of myocardial agents is the radioiodinated fatty acids where either iodine-123 or iodine-131 is the gamma-emitting label. Long-chain fatty acids are an important energy source for the myocardium and are efficiently extracted from the blood by the heart. These facts, coupled with both the short half-life of I-123 (13 hr) and its excellent gamma energy (159 keV), together with the convenient labeling of fatty acids by radioiodide displacement of ω-bromofatty acids, have led to experimental and clinical evaluation of radioiodinated fatty acids for myocardial imaging. Perhaps the most attractive feature of these tracers is their potential for directly probing β-oxidation, the primary fate of fatty acids in the myocardium.

The potential utility of this class of myocardial imaging agents was first demonstrated in dogs in 1964 by Evans et al. (*1*), who used iodine-131 introduced at the carbon-carbon double bond of oleic acid. Papers describing the effects of different radionuclides and their position have appeared. In dogs, Poe et al. (*2*) showed that terminally iodinated fatty acids are extracted as efficiently as the parent carbon-11 fatty acids. The myocardial extraction of fatty acids labeled by iodination at double bonds is reduced by approximately half relative to the parent carbon-11 fatty acid. In mice, Machulla et al. (*3*) showed that myocardial extraction of ω-halo fatty acids is more efficient than α-halo fatty acids where n ≥ 15. Of the nuclides studied, ω-I-123 fatty acid was comparable in extraction to the parent carbon-11 fatty acid, whereas ω-carried Br-77 and Cl-34m cases were reduced by approximately half. Terminally labeled iodofatty acids have since been evaluated as myocardial imaging agents (*4–6*).

The two major limitations to the use of straight-chain radiolabeled fatty acids lie in their rapid metabolic turnover in the myocardium and their high blood activity levels. Poe et al. (*7*) report that human images degrade rapidly after 20 min due to these limitations. The high blood activity levels are due almost entirely to free radioiodide, as shown by Feinendegen (*3*) and Poe (*7*). Both limitations seemingly result from rapid β-oxidation (high metabolic turnover rates) by the myocardium and liver. The high blood activity is the lesser limitation, since a subtraction technique for blood iodide proposed by Vyska et al. (*8*) improves image quality. Seven-pinhole tomography can also be used to improve image quality in the presence of high blood activity levels (*9*). Blood activity can also be chemically reduced by replacing the alkyl carbon-iodine bond with an aryl carbon-iodine bond, as shown by Machulla (*10*).

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One possible means of reducing myocardial turnover rates (increase $t_{1/2}$) is to promote myocardial storage of fatty acids as triglycerides. Erucic acid ($C_{22:1\omega13}$) has been shown to be stored in the form of triglycerides in the rat heart at various time intervals up to 30 min after injection (*11,12*).

The purpose of this investigation was to determine the effects of chain length on both myocardial extraction and the nature of retained activity. Six terminally radioiodinated (ω), fully saturated fatty acids ranging in length from C_{11} to C_{27} have been synthesized and tested in rats.

MATERIALS AND METHODS

Microanalyses were performed commercially.* Thin layer chromatography (TLC) was done on precoated, 250-μ cellulose† or silica gel plates.‡ The AG1-X8 anion exchange resin‖ (chloride form, 200–400 mesh) was also obtained commercially.

Proton magnetic resonance (PMR) spectra are reported in parts per million downfield from internal tetramethylsilane; infrared (ir) spectra were also obtained.

The following compounds or reagents were obtained from commercial sources: 11-bromoundecanoic acid, ω-undecenyl alcohol, 16-hydroxyhexadecanoic acid, 8-bromooctanoic acid, methylethyl ketone, and sodium iodide (I-125).

Tissue distribution studies. All radioiodinated fatty acids were evaluated in female Sprague-Dawley rats weighing 250–350 g. They were given food and water *ad libidum*. Tissue distribution studies were done using iodine-125-labeled fatty acids.

For these studies, approximately 25 μCi (~25 μg) of ω-[^{125}I]iodofatty acid in 0.25–0.30 ml of physiological formulation (EtOH/Tween 80/0.9% saline: 2.5 ml/0.65 ml/22 ml) were administered intravenously to ether-anesthetized rats. The animals, three for each time interval, were killed at preselected time intervals (5, 10, 20, and in some cases 40 and 90 min). Representative 50–100 mg samples of liver, lung, heart, blood, muscle, and thyroid were removed and cleaned of fat and connective tissue. Duplicate samples of each tissue were weighed on an analytic balance with computer printout, and prepared for counting. Samples were placed in test tubes together with distilled water and counted using an autogamma scintillation counter. All values are corrected for radioactive decay, counting efficiency, and background. The values of resulting tissue concentrations were normalized to a body weight of 1 kg and are therefore reported as % kg dose/g.

Synthesis of unlabeled compounds. *12-Tridecenoic Acid* (**2a**). Compound **2a** was synthesized by a malonic ester condensation using sodium diethyl malonate and 11-bromoundecene (*13*). Hydrolysis and decarboxylation by standard procedures yielded **2a**. The physical constants confirm literature data (*14*).

18-Nonadecenoic acid, 21-docosenoic acid, and 26-heptacosenoic acid (**4a, 5a, 6a**). The synthesis and physical constant data for **4a** and **5a** have been reported elsewhere (*15*).

Compound **6a** was synthesized by the same general procedure: mp 79–81; ir (CCl_4): 1642 (w) ($-CH{=}CH_2$), 1710 ($-CO_2H$), 2860 and 2930 ($-CH_2-$) cm^{-1}; PMR (CCl_4) δ: 1.07–1.5 (envelope centered at 1.23, 44H, $-C\underline{H}_2-$), 2.1 (m, 4H, $=CH-C\underline{H}_2-$ and $C\underline{H}_2-CO_2H$), 4.7–6.03 (m, 3H, $-C\underline{H}{=}C\underline{H}_2$), 11.9 (s, 1H, $-CO_2\underline{H}$).

13-Bromotridecanoic acid, 19-bromononadecanoic acid, 22-bromodocosanoic acid, and 27-bromoheptacosanoic acid (**2, 4, 5,** *and* **6**). Compounds **2a** and **4a–6a** were brominated with dry hydrogen bromide in the presence of benzoyl peroxide according to a published procedure (*16*). The purified products, compounds **2, 4,** and **5**, were characterized by PMR, ir, melting point, and elemental analysis. Literature values for **2** (*14*), **4** (*17*), and **5** (*18*) were confirmed. Compound **6** was characterized as follows: mp 79–81; ir (CCl_4): 1710 ($-CO_2H$), 2850–2860 and 2925–2930 ($-CH_2-$) cm^{-1}; PMR ($CDCl_3$)δ: 1.10–1.53 (envelope centered at 1.26, 46H, $-C\underline{H}_2-$), 1.5–2.5 (m, 4H, $-C\underline{H}_2CO_2H$ and $-C\underline{H}_2CH_2Br$), 3.41 (t, 2H, $-C\underline{H}_2Br$), 11.3 (s, 1H, $-CO_2\underline{H}$).

16-Bromohexadecanoic acid (**3**). Compound **3** was synthesized as previously described (*19*).

Synthesis of radiolabeled compounds. All radiosyntheses in this study were completed using the procedure outlined as follows.

Radioiodide exchange. The brominated fatty acid (3 mg) was refluxed for 1–5 hr in methylethyl ketone (4–5 ml) containing 3 mCi $Na^{125}I$ (no carrier added). The progress of exchange was followed by TLC (cellulose plates, n-hexane/diethyl ether/glacial acetic acid: 320/80/1; R_f fatty acid = 0.85–0.95, R_f $^{125}I^-$ = 0.0). The solvent was removed under a stream of nitrogen gas after the exchange was judged complete; typically >90% exchange was found by radiochromatographic scans of the TLC plates. The residue was formulated by dissolution in absolute ethanol/Tween 80, then diluting to volume with normal saline. To remove free radioiodide, the formulation was passed through a glass column packed with about 1.0 g AG1-X8 anion exchange resin (chloride form) and washed with formulation. Removal of free radioiodide was confirmed by repeat TLC on cellulose using eluent as above (R_f values as above). Isolated yields ranged from approximately 40% for **6** to 60–90% for other compounds. Specific activities ranged from 0.75–1.0 mCi/mg.

Purity determination. The radiochemical purity was greater than 95% as determined by radio-TLC on silica gel using n-hexane/diethyl ether/glacial acetic acid:

70/30/1 (R_f of fatty acid = 0.15, R_f of free radioiodide = 0.0), and on cellulose using n-hexane/diethyl ether/glacial acetic acid: 320/80/1 (R_f of fatty acid = 0.85–0.95, R_f of free radioiodide = 0.0). The radiolabeled compounds (**3–7**) were stable in formulation for at least 24 hr as determined by repeat TLC.

Analysis of the heart. This was performed as follows at 5 and 20 min for 16-[^{125}I]fatty acid and at 5 and 40 min for 19-[^{125}I]fatty acid. Three rats were injected as above for each time interval. Data at 5 min were obtained in order to assess early biological distribution. The tissue distribution data generated first suggested a longer retention time for radioactivity for n = 18 relative to n = 15. The 40-min evaluation period for n = 18 was chosen (rather than 20 min as for n = 15) to reflect the increased duration of radioactivity in the myocardium. The heart, rinsed free of blood, was divided into approximate thirds; each portion was weighed and counted to obtain 100% values. Each portion was then homogenized with 3.5 ml chloroform:methanol (2:1) using a microhomogenizer. The homogenate was transferred to a glass tube, 0.65 ml of a 40% aqueous solution of urea and 0.65 ml of 0.02 *N* H_2SO_4 added, and the tube vortexed for 1 min. After centrifugation, the phases were separated and chloroform removed from the organic phase by a stream of N_2. The pellet, aqueous, and organic residue fractions were counted in a gamma counter and the percentage of radioiodide activity relative to 100% value activity was determined.

The organic phase was redissolved in chloroform and separated by TLC on silica gel plates[§] (20 × 5 cm, thickness 250 μ) with n-hexane/methanol/chloroform (73.5:1.5:25). Tristearin served as triglyceride standard. The radioiodinated fatty acids served for fatty acid standards. The plates were developed in an iodine chamber. After visualization of the bands, they were carefully scraped from the plate and transferred to gamma tubes for counting. The remainder of the plate was divided into 1-cm sections and each section removed and counted. Most of the radioactivity (>70%) was associated with the visualized bands; R_f fatty acids = 0.0, R_f triglycerides = 0.20–0.30. Recovery data together with activity distribution between tissue pellet, aqueous, and organic phases are summarized in Table 1, which also presents control data for the extraction of each fatty acid from rat heart. A second chromatographic system, n-hexane/diethyl ether/glacial acetic acid (90:10:1) on silica-gel plates as above was also used. Fatty acids and triglycerides could be separated into bands by visualization in an iodine chamber. R_f differences between the iodofatty acids and triglycerides were too small to warrant confidence.

RESULTS AND DISCUSSION

Table 2 summarizes the tissue concentration of the ω-[^{125}I]iodofatty acids in the heart, liver, blood, thyroid, lung, and muscle of the rat. Maximum uptake (>0.30% kg dose/g) is observed for all iodofatty acids except when n = 26 at 5 min. High uptake values are observed at 5 min for n = 18 and n = 21: 1.05 and 0.79% kg dose/g, respectively.

Clearance of radioactivity from the rat myocardium for n = 10, 12, and 15 (**1, 2,** and **3**) is dependent on chain length, as expected (*5*). The general trend observed is that myocardial activity at t > 5 min increases as chain length increases. Clearance of radioactivity with time for n = 15, 18, and 21 (**3, 4,** and **5**) is shown in Fig. 1, which also illustrates the superior myocardial extraction of n = 18 and 21 relative to n = 15.

Thyroid values increase with time after injection for all iodofatty acids (Table 2), which is consistent with the expected release of free iodide in vivo. Normal β-oxidation should yield end products of iodoacetate for even-carbon chains and 3-iodopropanoate for odd-carbon chains. Both of these end products are expected to yield free iodide: iodoacetate by alkylation, 3-iodopropanoate by dehydrohalogenation. Rates of release are expected to be different for each fragment, but there are insufficient data in this study for rate evaluation. Thyroid uptakes indeed are similar for all fatty acids evaluated, suggesting that deiodination may be the same for all

TABLE 1. DISTRIBUTION OF ACTIVITY IN HEART HOMOGENATES (%)

Time	% pellet	% aqueous	% organic	% recovered
19-[^{125}I]iodononadecanoic acid				
5	6.1 ± 1.5	5.1 ± 1.3	61.8 ± 4.3	73.0 ± 4.2
40	6.5 ± 0.7	4.9 ± 1.0	58.6 ± 3.5	70.0 ± 3.2
control	3.9 ± 0.6	2.5 ± 1.0	72.0 ± 2.4	78.4 ± 2.1
16-[^{125}I]iodohexadecanoic acid				
5*	5.3 ± 0.8	30.5 ± 2.6	20.9 ± 2.6	56.8 ± 3.7
20	6.7 ± 3.3	23.9 ± 1.9	30.0 ± 4.2	60.6 ± 4.7
control	4.7 ± 0.8	7.4 ± 0.3	66.6 ± 4.3	78.7 ± 4.0

* Data are based on ten heart samples; all others on nine samples.

TABLE 2. ACTIVITY DISTRIBUTION DATA FOR ^{125}I-$(CH_2)_nCO_2H$ IN RATS AFTER I.V. INJECTION*

n	Time (hr)	Heart	Liver	Blood	Thyroid	Lung	Muscle
10	0.08	0.35	0.25	0.21	1.94	0.15	0.05
		(0.32–0.36)	(0.19–0.30)	(0.19–0.23)	(1.57–2.39)	(0.13–0.16)	(0.04–0.06)
(1)	0.17	0.14	0.21	0.18	3.21	0.12	0.05
		(0.11–0.15)	(0.14–0.26)	(0.17–0.19)	(2.36–4.08)	(0.09–0.15)	(0.04–0.06)
	0.33	0.10	0.15	0.17	5.16	0.10	0.05
		(0.08–0.13)	(0.12–0.20)	(0.15–0.19)	(3.36–6.79)	(0.09–0.11)	(0.05–0.07)
12	0.08	0.30	0.60	0.18	2.07	0.20	0.10
		(0.17–0.37)	(0.38–0.78)	(0.15–0.20)	(1.49–2.53)	(0.13–0.29)	(0.07–0.15)
(2)	0.17	0.26	0.53	0.14	2.85	0.18	0.10
		(0.22–0.31)	(0.36–0.67)	(0.13–0.16)	(2.17–3.73)	(0.12–0.23)	(0.09–0.11)
	0.33	0.21	0.32	0.17	4.23	0.13	0.09
		(0.13–0.38)	(0.26–0.38)	(0.13–0.19)	(2.71–6.29)	(0.10–0.21)	(0.05–0.18)
15	0.08	0.39	0.85	0.08	0.47	0.27	0.13
		(0.34–0.48)	(0.74–0.98)	(0.06–0.12)	(0.40–0.54)	(0.23–0.36)	(0.06–0.18)
(3)	0.17	0.35	0.65	0.10	2.07	0.32	0.13
		(0.31–0.41)	(0.53–0.75)	(0.09–0.10)	(1.65–2.28)	(0.23–0.41)	(0.10–0.20)
	0.33	0.33	0.50	0.09	2.45	0.30	0.18
		(0.28–0.37)	(0.42–0.55)	(0.09–0.11)	(2.03–2.91)	(0.27–0.34)	(0.14–0.21)
	0.67	0.21	0.31	0.13	6.53	0.17	0.10
		(0.16–0.28)	(0.26–0.36)	(0.12–0.13)	(4.96–9.41)	(0.14–0.20)	(0.08–0.12)
18	0.08	1.00	0.53	0.16	0.68	0.26	0.22
		(0.88–1.22)	(0.48–0.56)	(0.12–0.18)	(0.44–0.85)	(0.22–0.30)	(0.16–0.26)
(4)	0.17	0.91	0.43	0.11	1.32	0.28	0.15
		(0.87–0.97)	(0.32–0.55)	(0.09–0.12)	(1.08–1.52)	(0.24–0.30)	(0.14–0.18)
	0.33	0.67	0.35	0.16	3.83	0.22	0.18
		(0.63–0.69)	(0.30–0.37)	(0.14–0.19)	(3.36–4.29)	(0.21–0.23)	(0.14–0.21)
	0.67	0.70	0.31	0.15	4.89	0.20	0.18
		(0.56–0.78)	(0.24–0.35)	(0.14–0.15)	(3.32–5.99)	(0.14–0.22)	(0.15–0.19)
	1.5	0.29	0.17	0.11	5.99	0.18	0.14
		(0.26–0.32)	(0.15–0.17)	(0.10–0.12)	(5.37–7.19)	(0.13–0.24)	(0.12–0.15)
21	0.08	0.79	0.98	0.10	0.46	0.28	0.19
		(0.71–0.90)	(0.87–1.15)	(0.09–0.12)	(0.31–0.58)	(0.25–0.31)	(0.16–0.28)
(5)	0.17	0.50	0.68	0.15	1.11	0.13	0.13
		(0.47–0.52)	(0.63–0.72)	(0.14–0.16)	(0.79–1.76)	(0.12–0.14)	(0.12–0.14)
	0.33	0.47	0.60	0.15	1.77	0.11	0.14
		(0.40–0.54)	(0.54–0.69)	(0.15–0.16)	(0.88–2.44)	(0.10–0.12)	(0.12–0.15)
	0.67	0.34	0.42	0.14	6.79	0.10	0.12
		(0.32–0.36)	(0.38–0.46)	(0.13–0.15)	(2.30–9.34)	(0.10–0.12)	(0.11–0.13)
26	0.08	0.25	0.50	0.57	0.75	0.44	0.09
		(0.24–0.25)	(0.41–0.55)	(0.54–0.59)	(0.60–0.80)	(0.31–0.58)	(0.09–0.10)
(6)	0.17	0.21	0.49	0.39	1.50	0.62	0.07
		(0.18–0.24)	(0.38–0.64)	(0.37–0.42)	(1.06–2.09)	(0.29–1.20)	(0.06–0.09)
	0.33	0.14	0.41	0.32	5.24	0.30	0.05
		(0.12–0.15)	(0.35–0.47)	(0.31–0.36)	(3.54–7.62)	(0.24–0.35)	(0.05–0.06)

* % kg dose/g; average of 3 rats and (range).

fatty acids. It is not clear whether this deiodination is a result of β-oxidation or of hydrolysis, or a combination of both.

The possibility that higher retention of activity in the myocardium would result in decreased blood activity levels is not supported by data in this study. Blood values

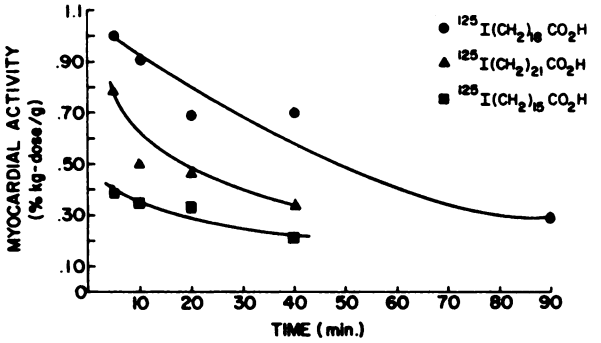

FIG. 1. Myocardial activity of iodofatty acids against time. Each data point represents three animals.

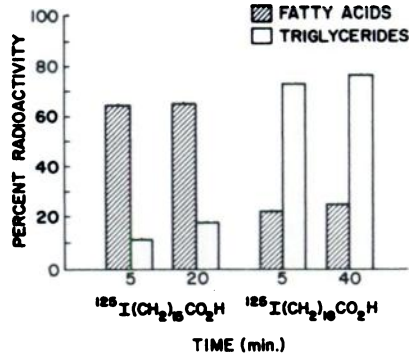

FIG. 2. Distribution of radioactivity between free fatty acids and triglycerides. Each bar represents three samples from each of three animals. Data for each time are calculated assuming initial activity in sample is 100%.

are comparable for all fatty acids evaluated except for n = 26. The increase for n = 26 may be attributed to lowered transport rates into heart and liver cells, or to increased protein binding in the blood.

Besides the myocardium, the liver is an important site for β-oxidation of fatty acids. The data presented in Table 2 show significant uptake of radioactivity by the liver; in most cases liver uptake exceeds myocardial uptake. Activity decreases with time (as with myocardial activity) which is consistent with β-oxidation. An approximate doubling of washout time is observed between n = 15 and n = 18. The amount of radioactivity at t = 5 min is diminished by half at about 30 min after injection for n = 15. For n = 18, 55–65 min are required for the same loss of activity. This change may reflect storage of n = 18 in triglycerides in the liver as for the myocardium (see following discussion).

Data for lung and muscle are presented to show the minimal uptake in these tissues. Fatty acid uptake in these tissues should not interfere with myocardial imaging.

Figure 2 shows the cellular distribution of radioactivity in the organic fraction at 5 and 20 min for 16-[^{125}I]iodohexadecanoic acid (**3**), and at 5 and 40 min for 19-[^{125}I]iodononadecanoic acid (**4**). The distributions of activity between pellet, aqueous, and organic fractions of the heart homogenates, together with percent recovery data, are given in Table 1. The other iodofatty acids were not examined in this fashion. Shorter-chain fatty acids (<16 carbons) are expected to undergo normal β-oxidation. The erucic acid analog (n = 21) has been shown to be in triglyceride storage (*11*, *12*).

Of the activity recovered, 64.7% ± 5.7 at 5 min and 64.8% ± 3.6 at 20 min was associated with the fatty acid band for the 16-[^{125}I]iodohexadecanoic acid. Activity (11.6% ± 7.4 at 5 min, and 17.1% ± 3.6 at 40 min) was also found in the triglyceride fraction. The 19-[^{125}I]-iodononadecanoic acid shows a markedly different cellular distribution of activity. Of the radioactivity recovered, 72.5% ± 8.1 at 5 min and 76.1% ± 6.7 at 40 min are in the triglyceride fraction. The amount of activity in the fatty acid fraction is 21.7% ± 6.2 at 5 min and 24.2% ± 6.8 at 40 min.

That thin layer chromatography is adequate to identify and to distinguish between free fatty acids and triglycerides as classes of compounds is amply supported in the literature. In particular, Gilbertson et al. (*20*) showed that cholesteryl esters and triglycerides could be distinguished from free fatty aldehydes, free fatty acids, and phospholipids where the lipids were obtained from heart-muscle homogenates. The homogenization, lipid extraction, and TLC procedures used by Gilbertson were adopted in this work. Thin-layer chromatographic systems were used as in the work previously published on the cellular distribution of erucic acid (*11*, *12*).

The longer myocardial residence time of radioactivity of both n = 18 and n = 21 compounds is attributed to storage of the ω-iodofatty acid as triglyceride. Based on the data presented here, the length of the carbon chain changes the cellular fate of the fatty acid from that of β-oxidation to triglyceride storage. The presence of a double bond at C-13 in erucic acid is apparently not necessary for triglyceride incorporation, since a saturated fatty acid of equal chain length (n = 21) is also stored.

The question of what the time course of the n = 18 and n = 21 compounds represent is not yet answered. The fact that some radioactivity is found in the free fatty acid fraction of cellular homogenates suggests that β-oxidation is occurring. Thus, the time course may reflect

TABLE 3. CHEMICAL STRUCTURES AND HEART-TO-BLOOD RATIOS AT 5 MIN

Structure	Heart/blood
[^{125}I]$(CH_2)_{10}CO_2H$	1.7
[^{125}I]$(CH_2)_{12}CO_2H$	1.7
[^{125}I]$(CH_2)_{15}CO_2H$	5.6
[^{125}I]$(CH_2)_{18}CO_2H$	6.5
[^{125}I]$(CH_2)_{21}CO_2H$	7.8
[^{125}I]$(CH_2)_{26}CO_2H$	0.45

turnover rates for triglycerides. In vivo deiodination of the triglycerides, with subsequent loss of label to blood pool, is not precluded as an explanation for the time course.

Heart-to-blood ratios at 5 min are listed in Table 3. To obtain myocardial rather than blood-pool images, heart-to-blood ratios should be as high as possible. The ratios for n = 18 and 21, the stored fatty acids, are higher than for n = 10, 12, and 26 and are marginally higher than for n = 15. These data suggest that in these terms, either n = 18 or n = 21 in an ω-iodofatty acid is at least equivalent to, if not potentially better than, n = 15 for myocardial imaging.

In conclusion, the chain length of ω-iodofatty acids has an effect on both myocardial uptake and length of time radioactivity remains in the myocardium (residence time). Increasing residence time should increase the length of time during which myocardial images can be obtained. Chain lengths of <17 carbons are metabolized rapidly by β-oxidation, as evidenced by short residence times and by association of radioactivity with the fatty acid fraction in the tissues for n = 15. Chain lengths of 19 and 22 carbons (n = 18 and n = 21) are stored in the myocardium in the form of triglycerides, thus increasing residence time relative to n = 15. The myocardial uptake is increased significantly for n = 18 and n = 21 relative to n = 15. Heart-to-blood ratios are also affected by chain length, with ratios being highest for those fatty acids that are stored as triglycerides.

The high myocardial extraction, longer retention of radioactivity, and concentration of activity in the form of triglycerides suggest that an ω-iodofatty acid with a carbon-chain length of 19 has potential for myocardial imaging where multiple projections are desired or where storage functions are being probed. For a metabolic probe of β-oxidation, a chain length of 16 or 17 carbons appears to be suitable.

FOOTNOTES

* Spang Microanalytical Laboratory.
† Analtech Cellulose CF.
‡ Analtech Silica Gel GF.
‖ Bio Rad.
§ Whatman KGF.

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