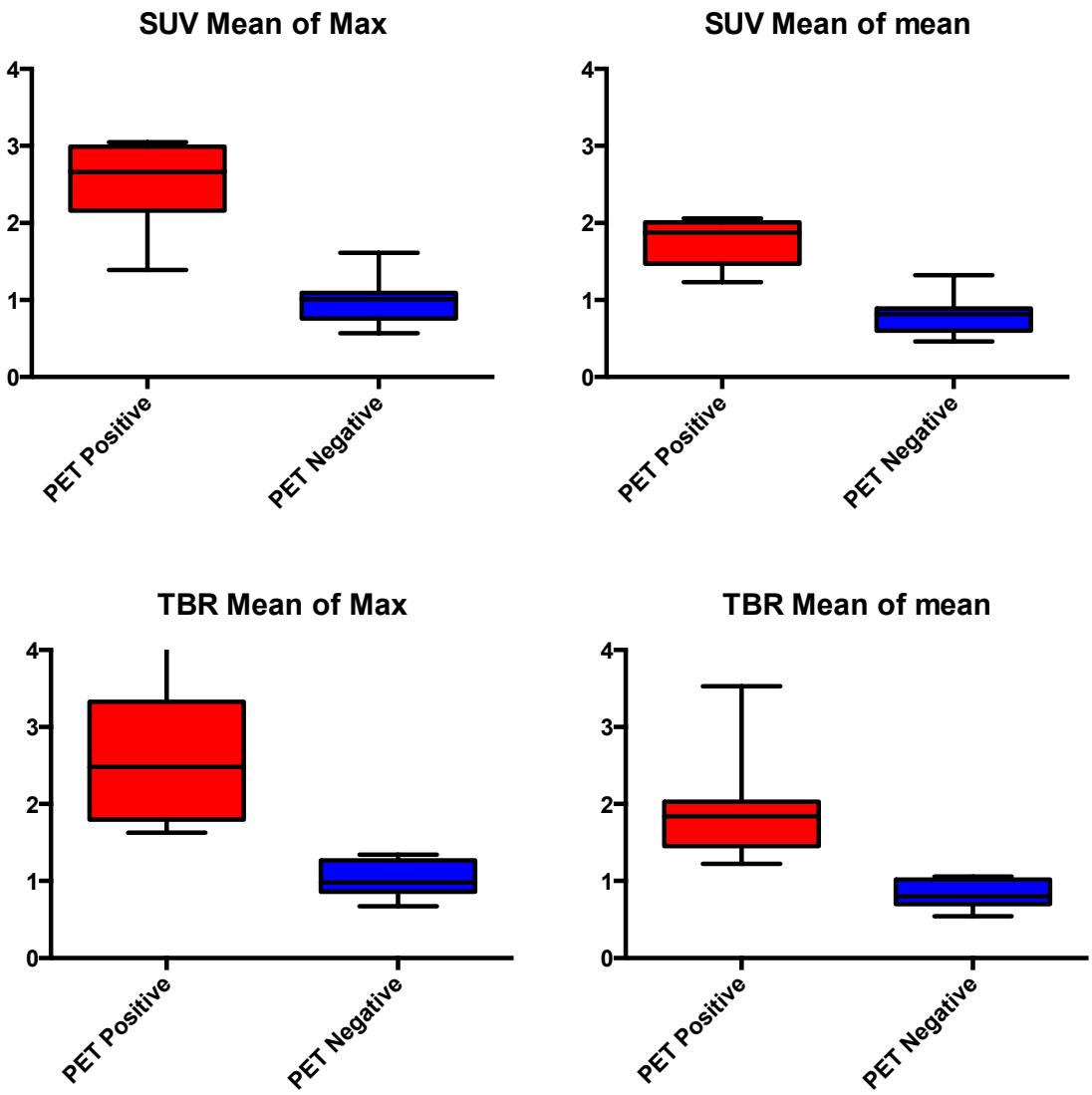
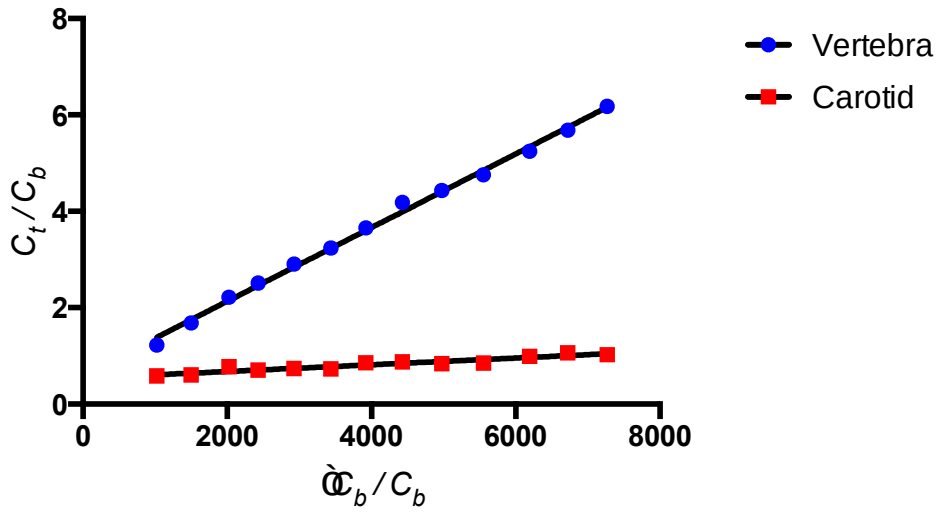
Supplementary Information

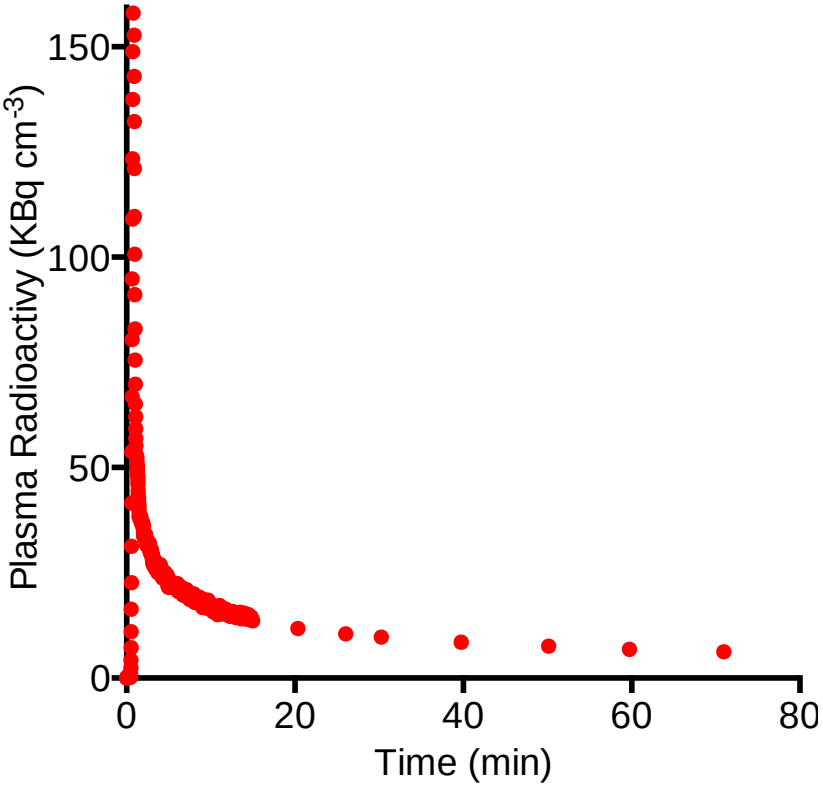
Supplementary Figure 1 The non-specific binding of ^{18}F-NaF is low.



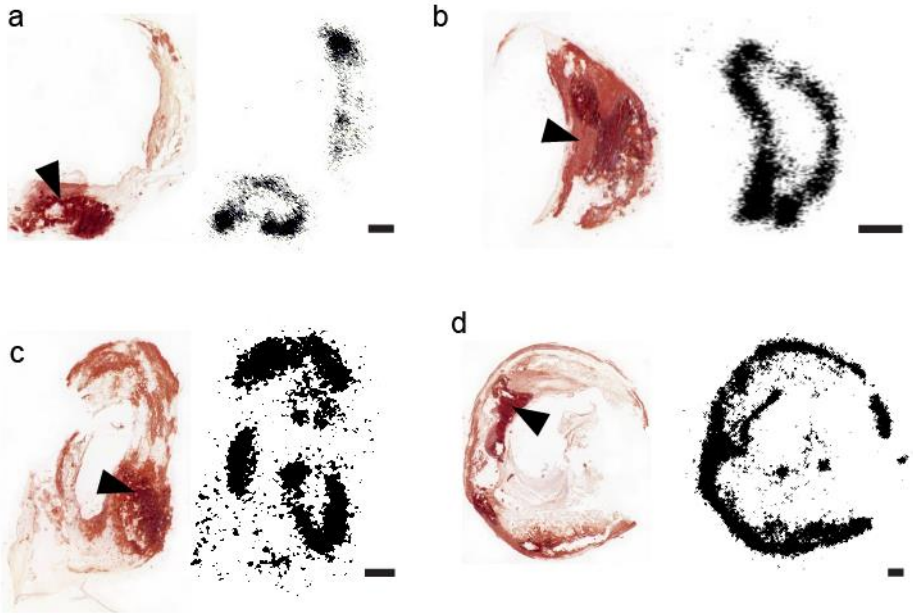
Supplementary Figure 2 Quantification of ^{18}F-NaF Uptake On Clinical Imaging. Box and whisker plots of Standardised Uptake Values and Target to Background Ratios for PET positive regions (red) and PET negative regions (blue) (Boxes show interquartile range, whiskers show range).



Supplementary Figure 3 Dynamic PET Analysis. Representative Patlak plots from a single subject showing vertebral and carotid uptake where C_b = plasma counts & C_r = counts within the region of interest.



Supplementary Figure 4 ^{18}F-NaF Pharmacokinetics. A typical arterial plasma activity curve (from a single patient) showing a very rapid redistribution and clearance of ^{18}F-NaF from the circulation.



Supplementary Figure 5 Additional representative examples of ^{18}F-NaF inability to penetrate deeper layers of macro-calcifications (closed arrowheads). Scale bar = 100 µm.

	O	P	Ca
Mean ± SD	77.76 ± 7.21	9.26 ± 2.73	12.98 ± 4.74

Native Sigma hydroxyapatite. Element concentration in atomic % (n= 51).

	O	P	Ca	F
Mean ± SD	76.01 ± 2.58	5.30 ± 2.78	7.48 ± 0.79	11.21 ± 1.30
F/Ca Mean ± SD	0.70 ± 0.26			

Sigma hydroxyapatite after incubation with 1% NaF for 8 hours. Element concentration in atomic % (n= 51).

	O	P	Ca	F
Mean ± SD	73.44 ± 2.81	7.91 ± 2.87	7.37 ± 0.73	11.28 ± 1.20
F/Ca Mean ± SD	0.90 ± 0.24			

Sigma hydroxyapatite after incubation with 1% NaF for 4 days. Element concentration in atomic % (n= 51).

Supplementary Table 1 EM analysis of hydroxyapatite standards to confirm co-localization of NaF.

Subject	Age	Sex	Neurovascular Syndrome	Duplex NASCET Stenosis	Days between symptoms and PET scan	Static or Dynamic Scan	Used for Micro/Clinical Comparison
1	88	Male	Stroke	65	10	Static	Yes
2	73	Female	TIA	80	13	Static	Yes
3	76	Male	TIA	85	26	Dynamic	Yes
4	59	Male	TIA	85	14	Dynamic	Yes
5	47	Female	Stroke	65	9	Dynamic	No
6	63	Female	Asymptomatic	60	n/a	Dynamic	No
7	76	Male	Asymptomatic	40	n/a	Dynamic	No

Supplementary Table 2 Patient demographics and basic imaging data.

Subject Number	PET Positive					PET Negative			
	SUV		TBR			SUV		TBR	
	Average Max	Average Mean	Average Max	Average Mean		Average Max	Average Mean	Average Max	Average Mean
1	2.66	1.47	3.33	1.84		1.01	0.82	1.27	1.02
2	3.05	2.06	1.80	1.22		1.61	1.32	0.95	0.78
3	2.75	1.94	2.48	1.75		1.09	0.89	0.98	0.80
4	2.99	2.01	5.26	3.53		0.76	0.60	1.34	1.06
5	1.39	1.23	1.63	1.45		0.57	0.46	0.67	0.54
6	2.30	1.88	2.24	1.84		0.88	0.71	0.86	0.70
7	2.16	1.70	2.57	2.03		1.06	0.82	1.26	0.98

Supplementary Table 3 Standardized Uptake Values and Target to Background Ratios for PET positive *versus* PET negative regions.

		Patlak	
		K_i [ml/cm^3/min]	**SE [%]**
Subject 1	Right Carotid	0.0063	12.7
	Left Carotid	0.0060	10.3
	Vertebra	0.0486	3.0
Subject 2	Right Carotid	0.0042	10.5
	Left Carotid	0.0028	7.1
	Vertebra	0.0459	1.8
Subject 3†	Right Carotid	0.0005	24.0
	Left Carotid	0.0009	34.1
	Vertebra	0.0431	2.8
Subject 4*	Left Carotid	0.0045	21.6
	Vertebra	0.0694	1.9
Subject 5*	Left Carotid	0.0068	28.2
	Vertebra	0.0649	3.4

Supplementary Table 4 Dynamic PET Analysis. K_i values for individual carotid plaques and vertebra. SE is standard error. Subjects 4 and 5 had no plaque in their right internal carotid arteries. The vertebral values are in agreement with previously published data. † Subject 3 had very little carotid plaque uptake. * Subject 4 and 5 K_i were estimated using image derived input functions.

	n, individual patients
Electron microscopy	10
Concentration-response curve	5
Time-activity curve	5
Histology	8
Dynamic PET scan	5
Translatonal clinical PET/CT to µPET/CT to Autoradiography/histology	4

Supplementary Table 5 Summary of patients involved in individual experiments.