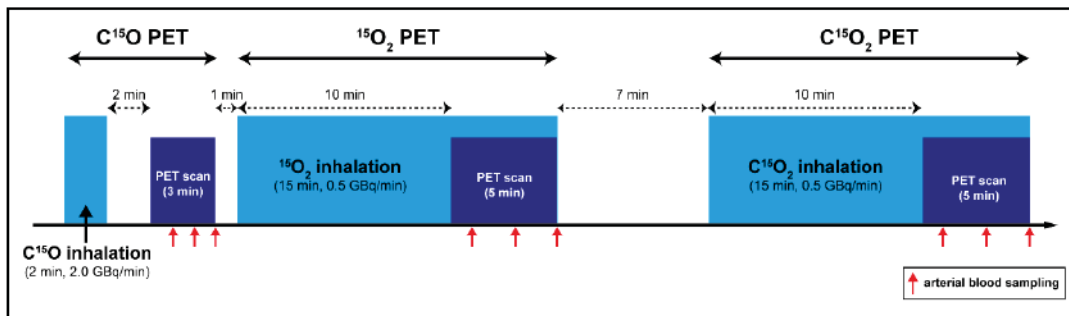
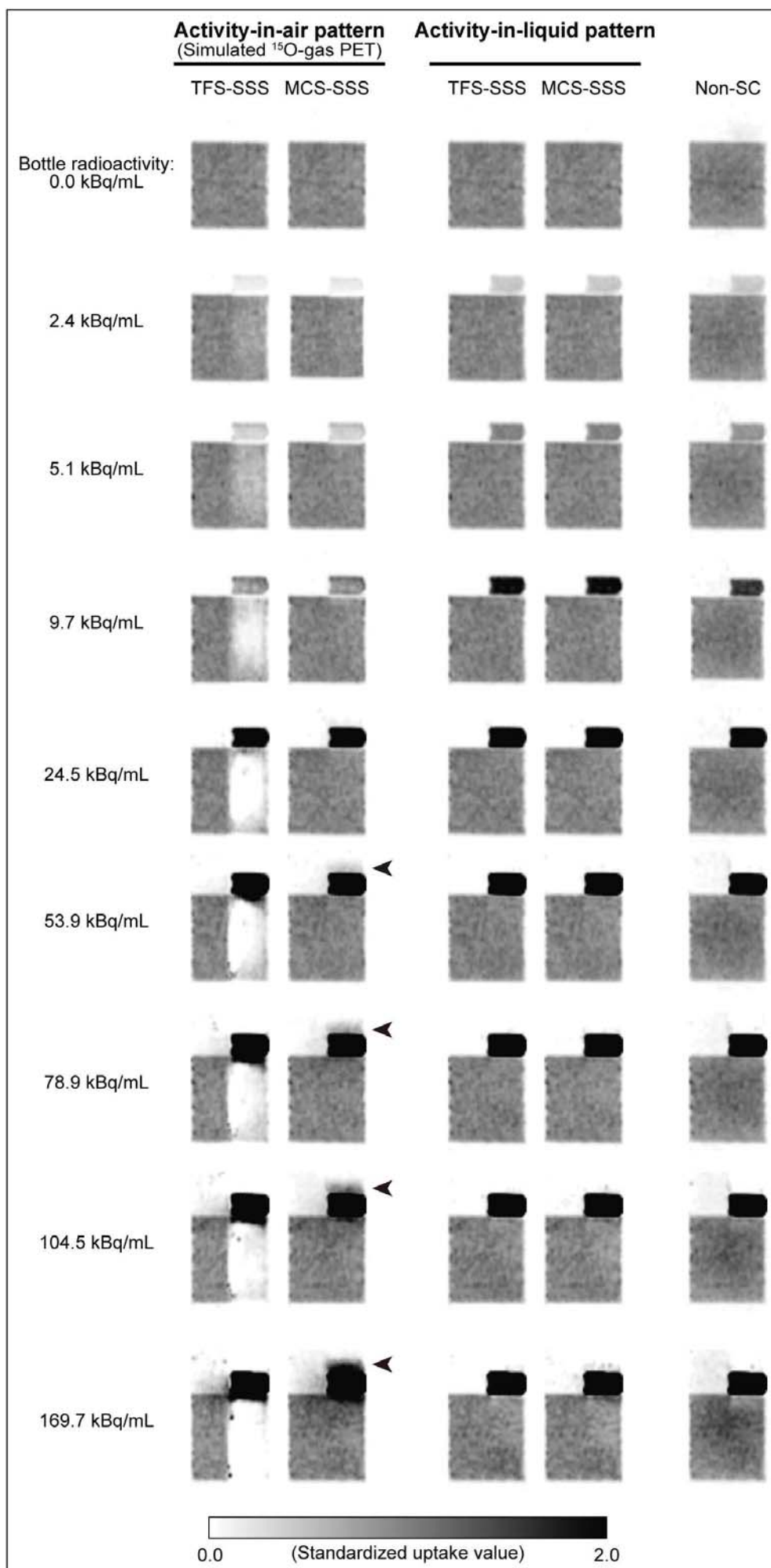


## MATERIALS AND METHODS

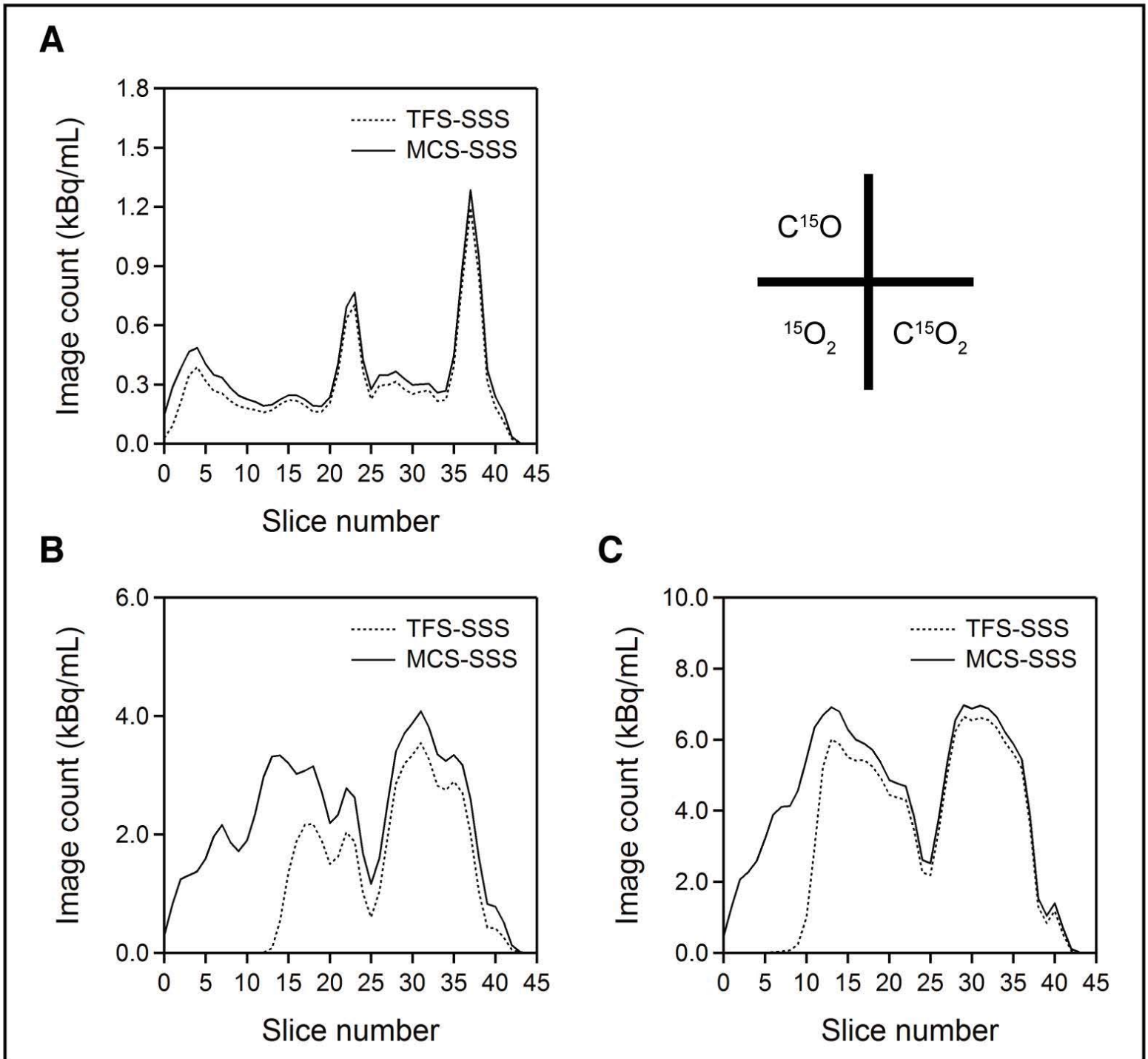
### Procedure for $^{15}\text{O}$ -gas Brain PET Scan Based on Steady-State Method

PET imaging was performed as follows. Three-minute static scanning was initiated 2 min after the end of 2-min  $\text{C}^{15}\text{O}$  inhalation (2 GBq/min), and arterial blood was sampled three times to measure the CBV during the scanning. After a 10-min continuous  $^{15}\text{O}_2$  inhalation (0.5 GBq/min), steady-state  $^{15}\text{O}_2$  images were acquired over a 5-min period, during which arterial blood was sampled three times to estimate OEF and  $\text{CMRO}_2$ . Finally, to determine CBF, steady-state  $\text{C}^{15}\text{O}_2$  imaging with three arterial blood samplings was performed over a 5-min period after a 10-min continuous  $\text{C}^{15}\text{O}_2$  inhalation (0.5 GBq/min).

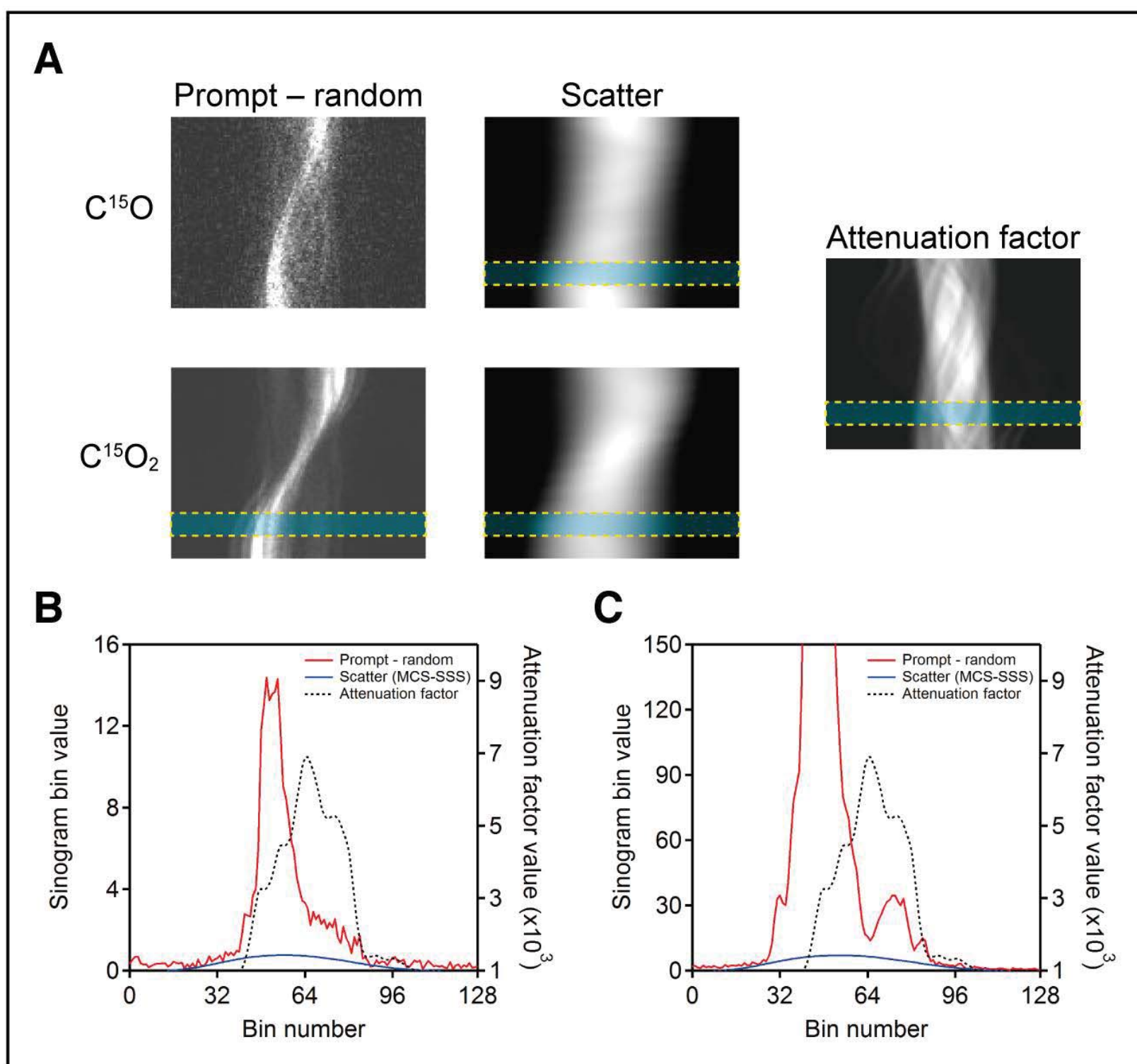




**SUPPLEMENTAL FIGURE 1.** Typical sagittal images of the phantom for the activity-in-air pattern which simulated  $^{15}\text{O}$ -gas brain PET, the activity-in-liquid pattern which simulated  $^{18}\text{F}$ -FDG PET, and the case without scatter correction, when the bottle activity levels were 0.0, 2.4, 5.1, 9.7, 24.5, 53.9, 78.9, 104.5 and 169.7 kBq/mL. Black arrowheads indicate the artifact above the plastic bottle.

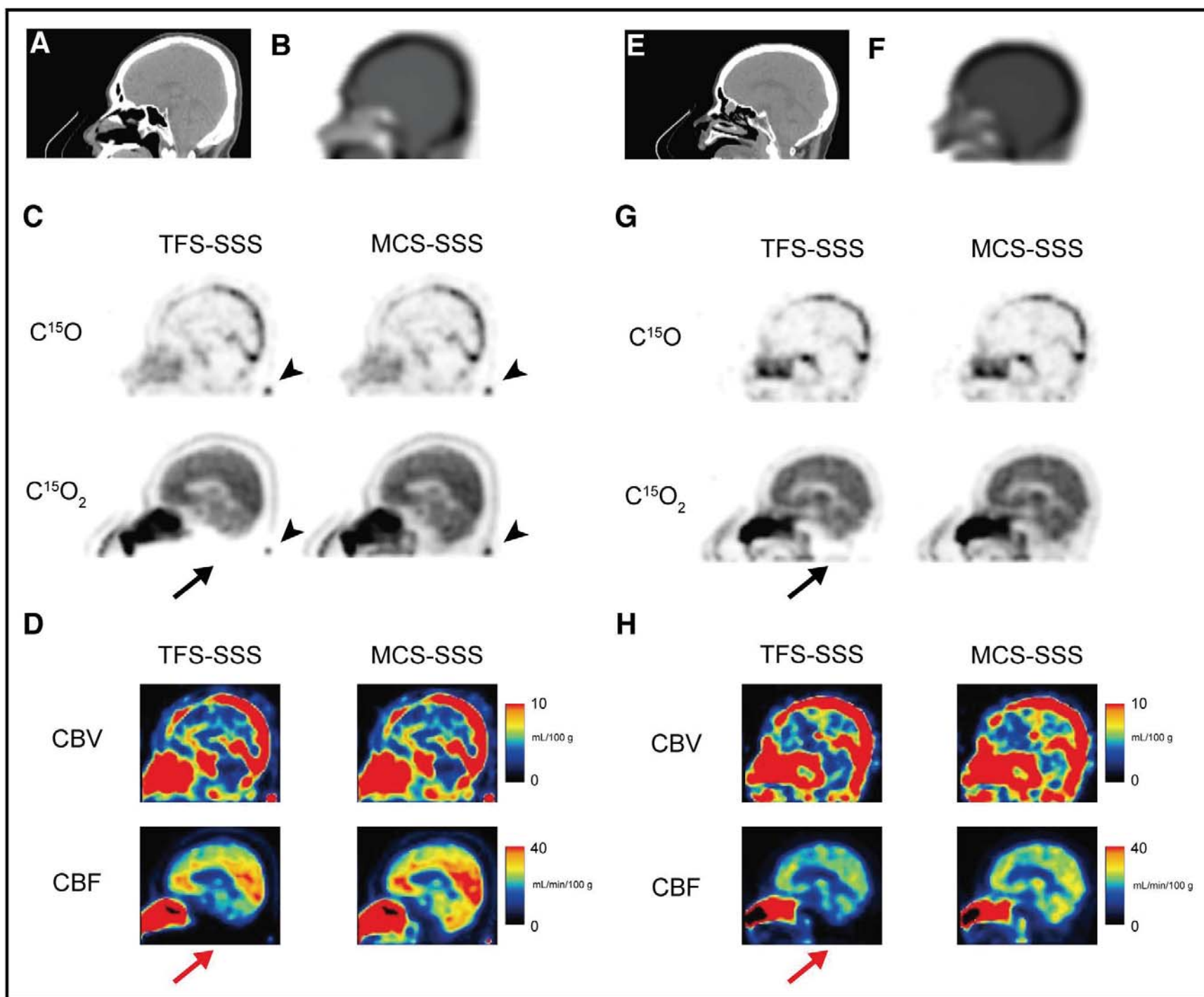


**SUPPLEMENTAL FIGURE 2.** Line profiles for the axial direction on sagittal images of the patient Case 1 for  $C^{15}O$  (A),  $^{15}O_2$  (B), and  $C^{15}O_2$  (C). The image counts were significantly smaller for slices with the face mask (slice# 0–10) on  $^{15}O_2$  and  $C^{15}O_2$  PET images reconstructed by TFS-SSS compared to MCS-SSS. For  $C^{15}O$ , image counts did not decrease even on the slices with the face mask in both TFS-SSS and MCS-SSS.

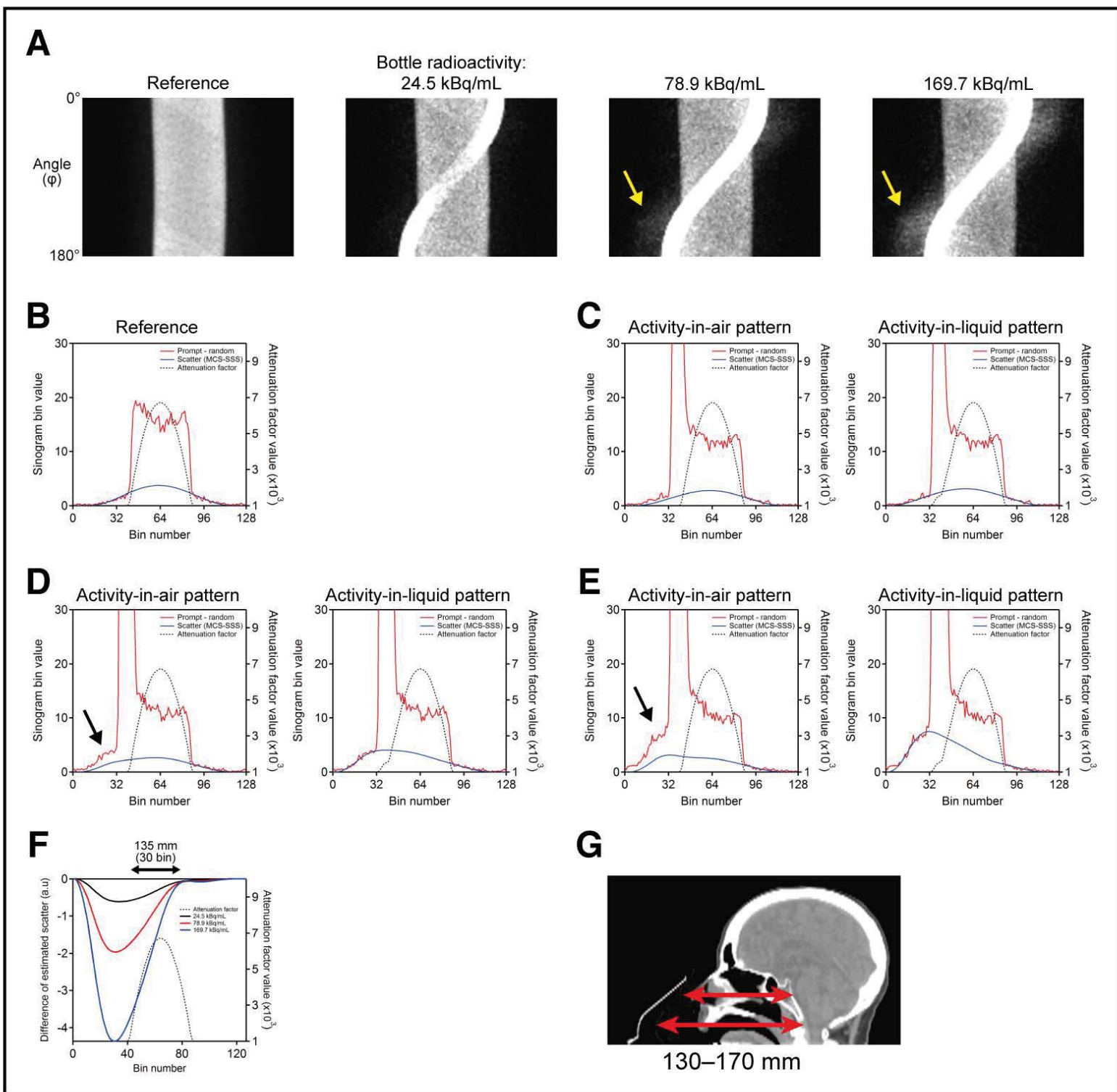


**SUPPLEMENTAL FIGURE 3.** Prompt – random (or true + scatter) sinograms, MCS-SSS-derived scatter sinograms for  $C^{15}O$  and  $C^{15}O_2$ , and attenuation factor sinogram (A). Average line profiles between yellow lines for  $C^{15}O$  (B) and  $C^{15}O_2$  (C), respectively.





**SUPPLEMENTAL FIGURE 4.** CT image (A,E),  $\mu$ -map (B,F), PET image (C,G), and the quantitative image (D,H) in the sagittal view of the other two patient cases. They had right (E–H) or left (A–D) internal carotid artery stenosis. Black arrowheads indicate the radioactivity of the  $^{15}O$ -gas supplying tube. As with the results of representative case (Figs. 4,5), the face mask is clearly shown in the CT image, but not in the  $\mu$ -map. In the  $C^{15}O_2$  PET image reconstructed by TFS-SSS and the CBF image derived from TFS-SSS, cold artifacts were generated on the slices with the face mask (black and red arrows). In contrast, the MCS-SSS image showed no artifacts. No artifacts were found on any images obtained with the inhalation of  $C^{15}O$  in both corrections.



**SUPPLEMENTAL FIGURE 5.** Prompt – random sinograms for the phantom studies on the slice with the plastic bottle at the bottle radioactivity levels of 24.5, 78.9, 169.7 kBq/mL and reference (filled with non-radioactive air in the plastic bottle for the CT and PET scans) (A). Yellow arrows indicate the scatters in the background region next to the high-radioactivity area. Average line profiles of the phantom for the reference (B), the activity-in-air and activity-in-liquid patterns at the bottle radioactivity levels of 24.5 (C), 78.9 (D), and 169.7 (E) kBq/mL. The profiles were averaged over all tilt angles ( $N = 7$ ) and drawn over 150.0–157.5 phi angle. The scatters in the regions next to the high-radioactivity area were underestimated in the activity-in-air pattern (black arrows). This underestimated scatters affected the artifact generation for the MCS-SSS-derived reconstructed images above the plastic bottle (Fig. 2, Suppl. Fig. 1). The difference of the estimated scatterers between activity-in-air and activity-in-liquid pattern at the bottle radioactivity levels of 24.5, 78.9, and 169.7 kBq/mL (F). The effect of the underestimated scatters was minimal in more than 70 bins position, which had the distance of 30 bins (= 135 mm) from the edge of high-activity region (40 bins position). Example CT image in the sagittal view of the patient Case 1 (G). The red two-way arrows indicate the distance between the face mask and the brain.

**SUPPLEMENTAL TABLE 1**

Coefficient of variation for activity-in-air pattern (%)

		Bottle radioactivity (kBq/mL)								
		0.0	2.4	5.1	9.7	24.5	53.9	78.9	104.5	169.7
Plastic bottle slice	TFS-SSS	6.9	9.1	12.7	43.9	142.0	268.8	252.9	281.1	—
	MCS-SSS	7.0	7.2	6.7	7.6	7.6	7.7	8.5	9.7	12.6
Non-plastic bottle slice	TFS-SSS	6.9	6.9	6.9	7.1	7.4	8.3	8.9	9.8	11.3
	MCS-SSS	7.0	7.0	7.0	7.3	7.5	8.2	8.6	9.2	10.6

— = Not available because the image counts were almost zero.

Coefficient of variation for activity-in-liquid pattern (%)

		Bottle radioactivity (kBq/mL)								
		0.0	2.4	5.1	9.7	24.5	53.9	78.9	104.5	169.7
Plastic bottle slice	TFS-SSS	6.6	6.7	6.4	7.3	7.3	7.2	8.1	9.2	11.5
	MCS-SSS	6.7	6.9	6.5	7.5	7.6	7.6	8.6	9.9	12.0
Non-plastic bottle slice	TFS-SSS	6.9	6.9	6.9	7.1	7.2	7.8	7.9	8.5	8.9
	MCS-SSS	7.1	7.1	7.0	7.3	7.5	8.0	8.3	8.8	9.0