Supplemental Data

Section 1: Estimation of transmission factors through stainless steel

The predominantly beta-emitting ^{204}Tl source (37 kBq) was purchased from Spectrum Techniques (Oak Ridge, TN). The beta transmission through 1 mm stainless steel, $\alpha_{\square}$ was estimated by acquiring RLI and block-RLI images of the ^{204}Tl source. Regions of interest (ROIs) were drawn over the source for both images, and mean intensities were calculated. α_1 = 1 – (block-RLI ROI intensity)/(RLI ROI intensity) for this system.

The gamma transmission, α_2, was estimated by acquiring RLI and block-RLI of ^{18}F-FDG (20 mL; 10.4 MBq (281 μCi) or 520 kBq/mL (14.1 μCi/mL)) within a 6 cm diameter glass petri dish that was covered by a 1 mm stainless steel slab. The stainless steel slab was assumed to block all betas, so that only gamma rays were detected within the RLI. For the block-RLI, the solution was covered by 2 mm stainless steel. α_2 = 1 – (block-RLI ROI intensity)/(RLI ROI intensity) for this system.

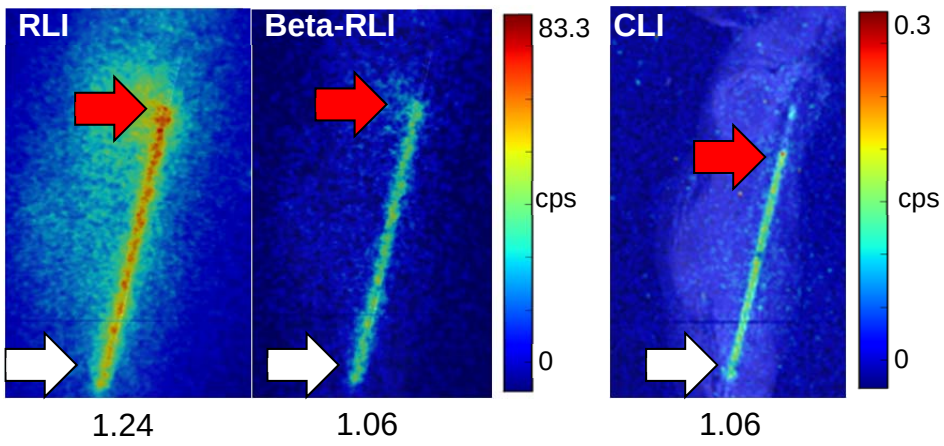
The radioisotopic screen (Bruker Biosciences Corporation, Billerica, MA) was used as the scintillator for these experiments. α_1 and α_2 were estimated as 0.03 and 0.91 respectively. The 3% beta transmission was expected, given that 2.9% of ^{204}Tl decay occurs through electron capture and gamma ray emission (347.5 keV) (*1*).

Section 2: Evaluation of candidate scintillators for beta-RLI

Beta-RLIs of the ^{18}F-FDG solution (20 mL; 10.4 MBq (281 μCi) or 520 kBq/mL (14.1 μCi/mL)) within the 6 cm diameter glass petri dish were obtained with the following scintillators: the radioisotopic screen, an autoradiography screen (BioMax TranScreen-HE; Carestream Health, Rochester, NY), and a 2 mm-thick plastic scintillator (RP-400 Rexon Components, Beachwood, OH), which had sufficient thickness for almost complete beta absorption (*2*). CLI was also acquired. Average intensities within ROIs placed over the solution were obtained. With respect to scintillator amplification, the radioisotopic screen, autoradiography screen, and plastic scintillator provided 470.0, 39.1, and 9.9-fold more photons per second than CLI.

Section 3: Signal uniformity over varying background

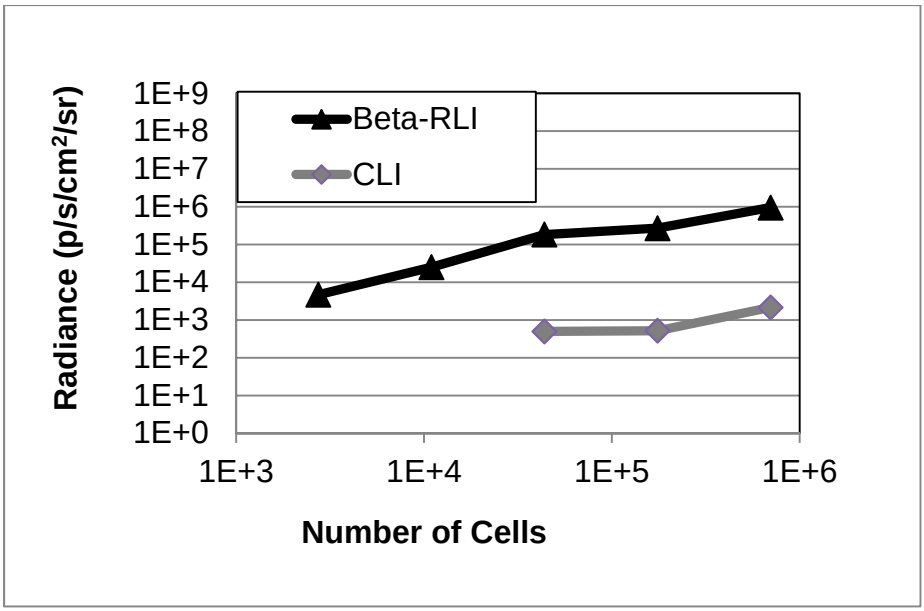
In order to analyze signal uniformity over a varying background, a 1 mm diameter capillary tube filled with 229 kBq/mL (6.2 μCi/mL) ^{18}F-FDG was placed under a mouse carcass. Prior to sacrifice, the mouse had been injected with ^{18}F-FDG, and the estimated activity at the time of imaging was ~3.7 MBq (~100 μCi) ^{18}F-FDG. The capillary tube was placed along the longitudinal axis of the mouse. The Bruker Xtreme (Bruker Biosciences Corporation, Billerica, MA) system was used, because the stage and platform holding the scintillator screen underneath were exactly parallel. The CCD camera imaged the mouse from below the stage. RLI, beta-RLI, and CLI were acquired. Small ROIs were placed along the superior and inferior aspects of the capillary tube. Ratios of mean superior ROI intensities to mean inferior ROI intensities were calculated. The ratios were 1.24 for RLI, 1.06 for beta-RLI, and 1.06 for CLI. As shown in Supplemental Fig. 1, beta-RLI was effective in suppressing gamma rays from a heterogeneous background.



Supplemental Fig. 1. Signal uniformity across varying background. A 1 mm diameter capillary tube filled with 229 kBq/mL (6.2 μCi/mL) ^{18}F-FDG was placed in front of a mouse carcass with ~3.7 MBq (~100 μCi) ^{18}F-FDG. RLI, beta-RLI, and CLI are shown. The number below each image represents the ratio of the superior ROI (red arrow) to the inferior ROI capillary tube (white arrow). Image scale in counts per second (cps).

Section 4: Serial dilutions of B16-F10 cells.

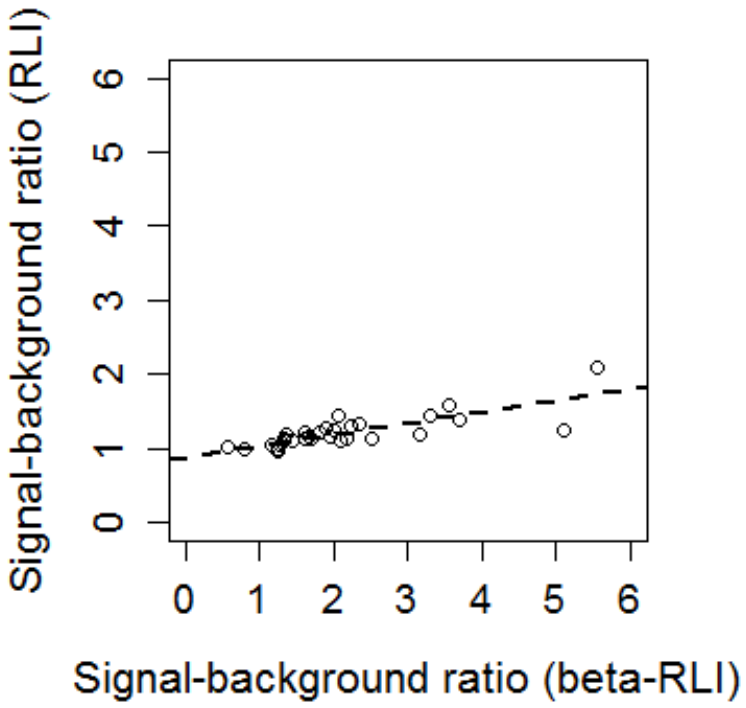
In order to determine the sensitivity of beta-RLI and CLI for detecting ^{18}F-FDG-avid cells, B16F10 cells and A375 cells were introduced to ^{18}F-FDG through the following steps. First, the cells were incubated in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin at 37°C in a 150 cm^2 T-flask (Thermo Scientific, Waltham, MA) overnight. The cells were then washed three times with phosphate buffered saline (PBS), and incubated in DMEM without glucose for 30 minutes. Next, ^{18}F-FDG was added to the solution to a target concentration of 300 kBq/mL (8.1 μCi/mL), and the cells were incubated for an additional 30 minutes. The cells were then washed with PBS three times, dissociated with 0.25% Trypsin-EDTA (Invitrogen Life Technologies, Carlsbad, CA), gently centrifuged, and counted under a microscope with a hemocytometer. Cells were then serially diluted by a factor of four to concentrations ranging between 1E3-1E6 cells in 50 μL solutions of 1:1 PBS:matrigel on microscope slides. The samples were then imaged on an IVIS system. As shown in Supplemental Fig. 2, beta-RLI was more sensitive than CLI across all B16F10 cell concentrations. For this cell line, photon sensitivity values, as calculated from the linear regression slope of radiance versus cell number, were 1.29 p/s/cm^2/sr/cell for beta-RLI and 0.0027 p/s/cm^2/sr/cell for CLI. For the A375 cell line, photon sensitivity values were 1.76 p/s/cm^2/sr/cell for beta-RLI and 0.0021 p/s/cm^2/sr/cell for CLI.



Supplemental Fig. 2. Radiance values of beta-RLI and CLI for serial dilutions of B16F10 cells.

Section 5: A comparative assessment of signal-background ratios for beta-RLI and RLI.

Among all tumors, the correlation coefficient between SBR values between beta-RLI and RLI was 0.80 ($p < 0.01$) (see Supplemental Fig. 3). The SBR for RLI (mean 1.21, standard deviation (sd) 0.21) was significantly less than that for beta-RLI (mean 1.81, sd 1.15), based on a one-sided t-test ($p < 0.05$). These results suggest that gamma rejection is needed for providing a sufficient SBR for tumor visualization.



Supplemental Fig. 3. SBR values for RLI versus beta-RLI. The dotted line represents the linear regression curve.

References:

1. Firestone RB, Ekstrom LP. WWW Table of Radioactive Isotopes. 1999. http://ie.lbl.gov/toi/. Accessed March 11, 2015.

2. Levin CS, MacDonald LR, Tornai MP, Hoffman EJ, Park J. Optimizing light collection from thin scintillators used in a beta-ray camera for surgical use. *Nucl Sci IEEE Trans On*. 1996;43(3):2053-2060.