

# Analytical Image Fusion in the Detection of Intrahepatic Hepatocellular Cancer

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## Abstract

**Purpose:** Since HCC lesions are generally characterized by lower Hounsfield unit value (HU) values and higher tracer uptake (SUV or Standardized Uptake Values), we intended to determine if normalizing the SUV by the HU, for the lesion and normal liver would improve sensitivity and specificity. **Material and Methods:** Twenty-three consecutive patients with HCC diagnosed clinically or pathologically underwent C11-Acetate (C11-A) and F18-FDG (FDG) PET/CT imaging before surgery during a 424-day interval. After exclusion of treated or calcified lesions, 44 lesions are included in this study. The original metrics are the maximum SUV (SUV<sub>max</sub>) and maximum or average HU (HU<sub>max</sub> or HU<sub>mean</sub>) for lesions and normal liver. For the normal liver, an average SUV (SUV<sub>mean</sub>) was included. The derived values are the ratios of SUV/HU values. The efficacy is the fraction of outcomes of non-overlapping metrics between lesion and normal liver. **Results:** For FDG the efficacy is 0.489 for the lesions SUV<sub>max</sub> versus normal liver SUV<sub>max</sub>. For lesion SUV<sub>max</sub>/HU<sub>mean</sub> versus normal liver SUV<sub>max</sub>/HU<sub>max</sub>, the efficacy is 1.00. For C11-A the corresponding values are 0.045 and 0.920. **Conclusion:** Normalizing SUV values for changes in HU values increases the contrast between normal liver and lesions. Analytical fusion can be very effective.

## Keywords

HCC (Hepatocellular Cancer)

## 1. Introduction

FDG PET/CT (Fluorodeoxyglucose Positron Emission Tomography combined with Computed Tomography) has not been widely used clinically for some cancers such as Hepatocellular Carcinoma (HCC) due to low level of FDG uptake within the lesions, associated with a high false negative rate. <sup>11</sup>C-Acetate (C11-A)

has been reported to have higher sensitivity but precise data on tumor size and differentiation are sparse.

Even so, the contrast between FDG and C11-A, across sizes and differentiation is striking. Across sizes, there is an average sensitivity of 0.46 for FDG and 0.79 for C11-A ( $p < 0.04$  in paired two tailed t-test) [1] [2] [3]. The effect of size is difficult to estimate because most authors express the sizes as ranges in arbitrary intervals. Even so, for intervals between 1 and 2 cm diameter, the sensitivity for FDG is 0.174 and for C11-A 0.870 [1]. In another reference [2], the respective sensitivities are 0.273 and 0.318. At larger sizes, the contrast between FDG and C11-A decreases (0.929 versus 0.952 respectively) [2].

Differentiation of the tumor also influences the detection rate of FDG but inconsistently: the rate is 0.00 [4], 0.356 [5] and 0.594 [6] for well-differentiated lesions. For poorly differentiated ones, the rates are 1.0 [4] and 0.895 [6]. With C11-A, the rates are 0.615 for moderately differentiated lesions and 0.848 for poorly differentiated ones [7].

The comparisons are not very valid because the threshold for positivity is arbitrary. The most common one is a ratio of 1.2 in comparison with the liver SUV or an SUV of 3.0 both for FDG and C11-A [1] [3] [7].

Dominique Delbeke [8] suggested in invited commentary that utilizing both tracer and categorizing positivity by a logical “OR” combination would present an advantage. However, the fractional rate gain of detection is very small, varying from 1.72% to a maximum of 12.7%. This is true for all lesions [1] [3] and patients [9]. The gain is low because the results of the two procedures are correlated. If they were independent, the gain by adding C11-A to FDG would be 41% and to add FDG to C11-A would be 5%. As it is, the combination does not increase efficacy perceptibly and would decrease efficiency.

In this paper, we present an analytical fusion approach whose goal is to improve the contrast between lesions and normal liver by utilizing information from the CT part of the PET/CT. This information is the density of the lesions or the normal liver expressed as Hounsfield Units (HU). HCC lesions have generally a lower HU value than normal liver [10]. The lesion SUV would relatively increase by the division by the lesion HU and the normal liver SUV would relatively decrease by a division by the normal liver HU. The operation would result in increased contrast.

## 2. Materials and Methods

Patient data are totally masked, including the date of the study, the sex of the patients and age. No patient consent was obtained.

Twenty three consecutive patients with HCC diagnosed clinically or pathologically underwent C11-Acetate and F18-FDG PET/CT imaging before surgery during a 424-day interval. The studies consists of two sets of images for each visit: First, 11 minutes after the injection of C11-acetate we acquired a non-iv-contrast CT and PET scan of C11-A, from skull base to the upper thighs. Forty-five minutes later, we injected F18-FDG. Imaging consisted again of a whole body

PET-CT scan from the skull base to the upper thighs, after 60 minutes uptake time without iv-contrast. Reconstructed images are reviewed in the axial, coronal, and sagittal planes.

After the exclusions of post-embolization lesions, 52 lesions from 23 patients were originally included in this study. We then excluded two hyper-perfused vascular shunt areas radiologically defined as vascular lesions. Later we excluded five lesions with a negative average HU value and one lesion with missing information. That left 44 lesions.

We measured the maximum SUV (SUVmax) for the lesions. For the normal liver we measured SUVmax and an average SUV value (SUVmean). Using the same regions of interest, we measured the average and maximum HU values from the non-contrast CT. We normalized SUVmax and SUVmean values by dividing them by the regionally corresponding HU values (HUmax and HUmean). Normal liver background originated at the peripheral regions to avoid large hepatic vessels and biliary ducts.

On the non-iv-contrast CT scan, the early HCCs are generally iso-dense compared to the normal liver background. As HCC progress, it becomes more hypodense if not fatty [10].

For the lesions, the metrics are the SUVmax as such and divided by the lesion's HUmax and HUmean. For the lesions, that makes it one original and two derived metrics (normalized values).

For the normal liver the metrics are the SUVmax and the SUVmean, each divided by the normal liver HUmax and HUmean. That makes two original metrics and four derived metrics (see **Table 1**).

The data are restricted to confirmed HCC lesions and normal liver. There is no additional comparison with the uptake in other lesions.

**Table 1.** Column 1 shows the ratios for the lesions e.g. SUVmax/HUmean is the ratio of the SUVmax over the average lesion HU. Column 2 uses the same code, but includes an average SUV for the normal liver regions. The efficacy is the fraction of the quantitative outcomes without overlap for lesion and normal liver values.

Lesion	Normalisation		Efficacy	
	Normal		C11-A	FDG
SUVmax	SUVmax		0.045	0.489
SUVmax	SUVmean		0.079	0.693
SUVmax/HUmax	SUVmax/HUmax		0.103	0.636
SUVmax/HUmax	SUVmax/HUmean		0.000	0.102
SUVmax/HUmax	SUVmean/HUmax		0.216	0.807
SUVmax/HUmax	SUVmean/Humean		0.000	0.148
SUVmax/HUmean	SUVmax/HUmax		0.92	1.000
SUVmax/HUmean	SUVmax/Humean		0.227	0.818
SUVmax/HUmean	SUVmean/HUmax		0.943	1.000
SUVmax/HUmean	SUVmean/Humean		0.352	0.977

The efficacy is the fraction of the cases in which the HCC metrics and the background metrics do not overlap. As an example for FDG, of the 44 lesions, 31 have a SUVmax larger than all the normal liver SUVmax values and 12 of the 44 normal liver SUVmax values are smaller than the smallest HCC SUVmax values. The efficacy or total of unambiguous results are 43 out of 88 observations or 48.9% efficacy.

### 3. Results

In general, our data correspond to those in the reviewed literature: If the threshold for the lesions, SUVmax is a SUV of 3.0, the sensitivity for FDG is 0.59 and 0.84 for C11-A. However, if a lesion/normal liver ratio larger than 1.2 is considered positive, the sensitivity for FDG is 0.65 (max/max) and 0.91 (max/mean) and for C11-A 0.61 and 0.77 respectively. However, our data do not support the concept that the limits should be the same for different tracers. For FDG the lesion SUVmax average is  $3.9 \pm 2.0$  and the normal liver SUVmax  $2.0 \pm 0.3$  and SUVmean  $1.7 \pm 0.3$ . For C11-A the corresponding values are  $4.9 \pm 2.5$ ,  $3.4 \pm 1.7$  and  $2.9 \pm 1.5$ .

To get equal sensitivities for FDG and C11-A, the lesion's FDG SUVmax limit should be lowered to 2.4, and the C11-A max/max lesion to liver ratio should be lowered to 1.18 and for SUVmax/HUmean to 1.00.

The normalization with the mean and maximum HU values has a profound effect for both tracers, but in general, yields better values for FDG (Table 1).

### 4. Discussion

The imaging detection of HCC is difficult because the intrahepatic lesions are competing with a relatively high liver background. It is noteworthy that the image of the radioisotope distribution is reconstructed with the inclusion of the CT portion of the procedure. However, the CT data seem to be used exclusively either to explain abnormal tracer uptakes by defined anatomical structures, or to detect abnormal structures that can be characterized by the tracer uptake.

Putting strict numerical limits on SUVmax values between normal and abnormal is problematic; the SUV values do not take into account that the distribution of the tracer is also influenced by the presence of competitive avid sites, including the kidneys, other FDG avid lesions and cardiac uptake for FDG. The lesion to liver ratio is in principle not influenced by those factors, but there is no a priori reason to assume that the ratio is independent of the nature of the tracer.

We demonstrate in this paper that using this prior information analytically improves the interpretation in the case of HCC. In general, there is more information in the fusion of images with different modalities or tracers than the purely visual [11] [12] [13] [14] [15]. Analytical fusion techniques were used to determine toxicity and dosimetry in treatment of liver tumors [11] [12] [13], evaluation of disease progression [14] and brain malignancies [15].

## 5. Conclusion

Analytical analysis of multiple modality imaging will improve the quality of diagnostic imaging.

## Clinical Relevance Statement

Multiple tracer imaging used analytically: Lam, M. G., Goris, M. L *et al.*, Prognostic Utility of Y-90 Radio-embolization Dosimetry Based on Fusion of MAA-Tc-Colloid SPECT. *J Nucl Med.* 54: 2055-61.

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