On the Need for Dynamic Segmentations in Quantitative Dynamic Nuclear Medicine

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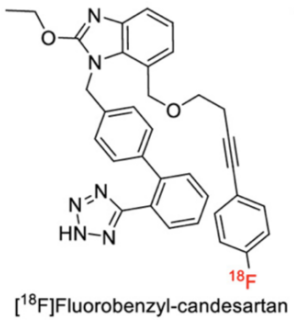
Overview

General Context: The Medical Aspect

- A drug, Candesartan, was synthesized with ^{18}F. This drug is used for renal hypertension;
- The radiolabelled drug would be used to verify whether the drug would be useful for a given patient;
- For acceptance by Health Canada, it must first be shown that the radiopharmaceutical drug binds

Health Canada Santé Canada

- A preclinical run was made on rats and mice at two Canadian institutions.



[^{18}F]Fluorobenzyl-candesartan

Figure: [^{18}F]fluoropyridine-candesartan

General Context: The Inception

- The left kidney of the animals had to be analyzed for pharmacokinetic parameters;
- The reference tool used would have been the Task Group 211 (TG-211) Report from the American Association of Physicists in Medicine (AAPM);
- The proposed methods are static and don't consider metabolic and physical movements of the subjects between timeframes.

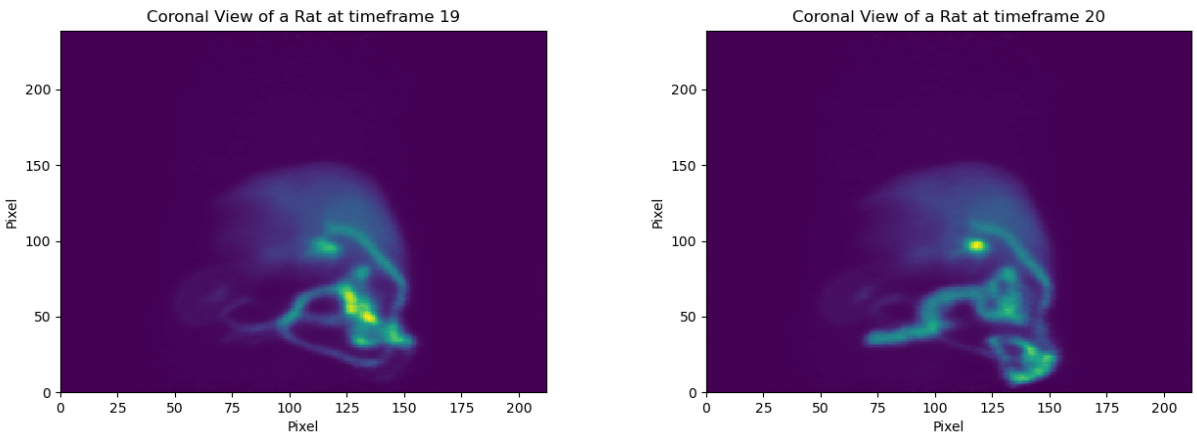


Figure: Two temporally adjacent timeframes for a PET acquisition on a rat

New Goal

- The new goal is to understand the impact of a static segmentation on a dynamic PET image;
- This would lead to a better understanding of:
  - Methodological Errors;
  - Impact of the segmentation method;
  - Impact upon the subsequent analyses (qualitative and quantitative).

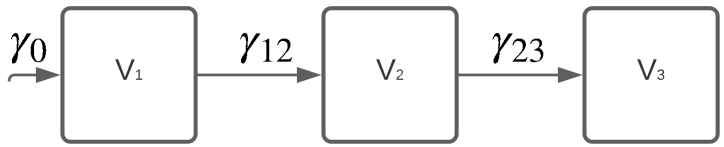


Figure: Schematic Representation of the phantom

Experimental Approach: Theoretical Model

- A simple two-compartment model is regulated by the following set of differential equations:

$$\begin{bmatrix} Q_1' \\ Q_2' \\ Q_3' \end{bmatrix} = \begin{bmatrix} -\frac{\gamma_{12}}{V_1} & 0 & 0 \\ \frac{\gamma_{12}}{V_1} & -\frac{\gamma_{23}}{V_2} & \\ 0 & \frac{\gamma_{23}}{V_3(t)} & 0 \end{bmatrix} \begin{bmatrix} Q_1 \\ Q_2 \\ Q_3 \end{bmatrix}$$

- This model can be analytically solved for the two first compartments, which are of interest:

$$C_1(t) = \frac{Q_0}{V_1} e^{-\frac{\gamma_{12}}{V_1} t}$$

$$C_2(t) = Q_0 \left(\frac{\gamma_{12}}{\gamma_{23} V_1 - \gamma_{12} V_2} \right) \left[e^{-\frac{\gamma_{12}}{V_1} t} - e^{-\frac{\gamma_{23}}{V_2} t} \right]$$

Experimental Approach: Experimental Model

- In order to understand the limitations of static segmentations in dynamic imaging, a custom phantom was made;
- The phantom had three compartments with the two of interest;
- Many dynamic acquisitions were done with FDG.

Figure: X-ray view of the phantom

Analysis: First Steps

- With the images, we took a subsample (4-D subset of the image) of it containing the compartment of interest;
- We did various segmentations based on the AAPM TG-211 categories (statistical, gradient, and filling);
  - The segmentation were done on a given timeframe and kept constant for the whole dynamic acquisition;
- We selected by hand the segmentations that gave a roughly desirable shape.

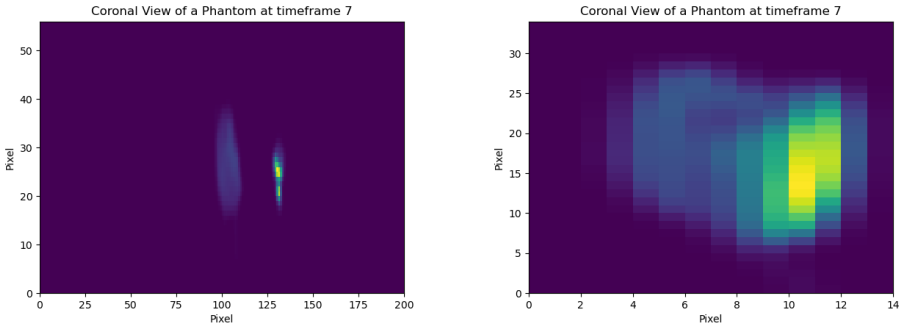


Figure: Left: A top view of a given dynamic acquisition at a given timeframe
Right: The subset for the second compartment (right)

Analysis: The Segmentations

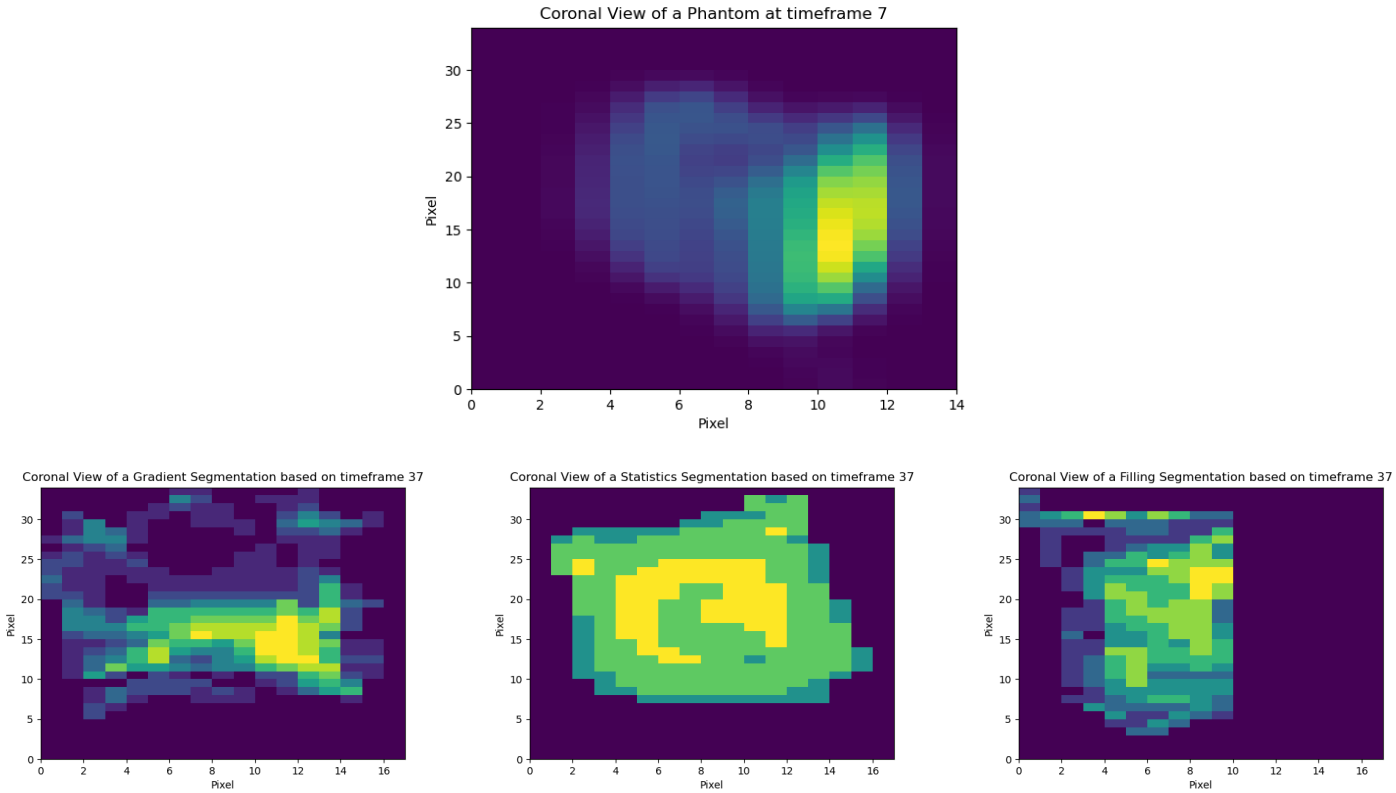


Figure: Top: Reconstructed Image centered around the second compartment for a given timeframe;
Bottom: Segmentations of the top image based, respectively, on gradients, statistics, and filling methods.

Analysis: The Tools

- To analyze the results and the quality of the segmentations, three quantitative tools were used:
  - Dice Coefficients;
  - TACs with shifting errors;
  - Pharmacokinetic parameters from the TACs.
- For the two last methods, an uncertainty was introduced into the TACs by moving subtly the segmentations by one voxel.

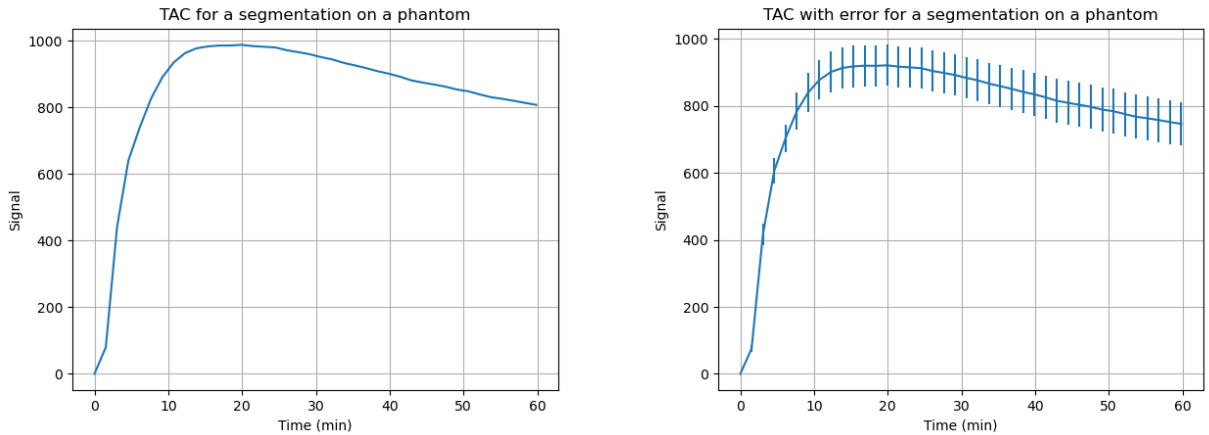


Figure: Left: TACs as obtained directly
Right: TACs with the introduced uncertainty

Analysis: Sørensen-Dice Coefficient

- The Sørensen-Dice coefficient can be used to compare two segmentations;

$$D(A, B) = \frac{2|A \cup B|}{|A| + |B|}$$

- For a given segmentation, the segmentations based on different timeframes were compared.

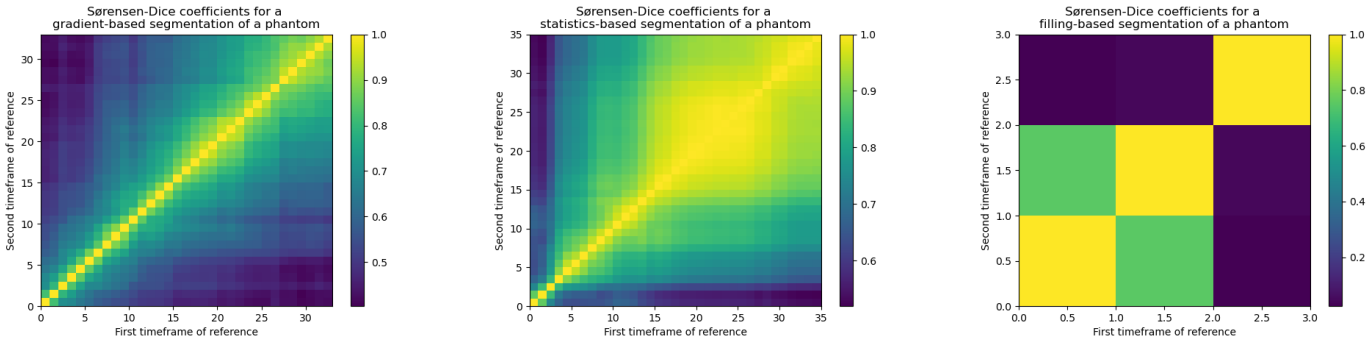


Figure: Dice Coefficients for a given dynamic acquisition based on many timeframes.
N.B.: The number of decent segmentations varied greatly with the method.

Analysis: TACs

- The TACs were qualitatively compared to see whether they overlapped in their uncertainties;
- For the phantom, this was the case for most of the acquisitions.

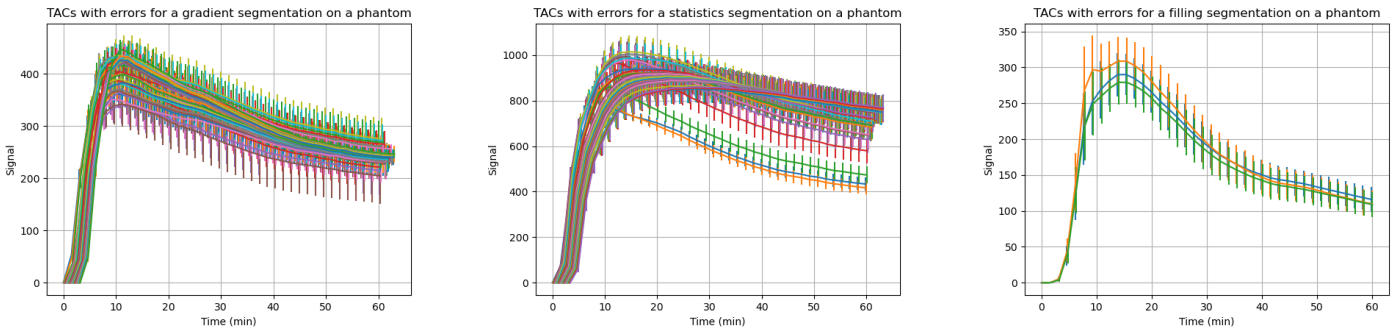


Figure: TACs with uncertainties for a given acquisition. In this case, most of the TACs overlap.

Analysis: Pharmacokinetic Parameters

- By using the two-compartment model, it is possible to estimate the pharmacokinetic parameters;
- This extraction was made using the *Dynesty* package in *Python*.

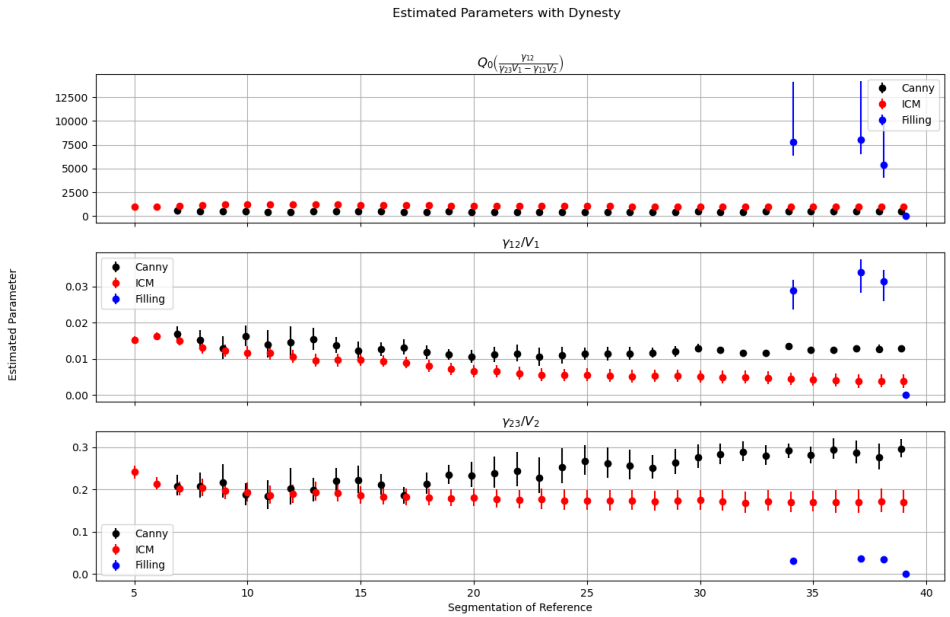


Figure: Pharmacokinetic parameters obtained via *Dynesty* for a specific dynamic acquisition.

Summary

- The results so far indicate that static segmentations are not adequate for dynamic acquisitions, even in the simplest case;
- For preclinical dynamic images, more work needs to be done;
- Possible future endeavours include:
  - The use anatomical images;
  - The use of segmentations valid for dynamic images;
  - The integration of sufficient uncertainties in the proposed results.

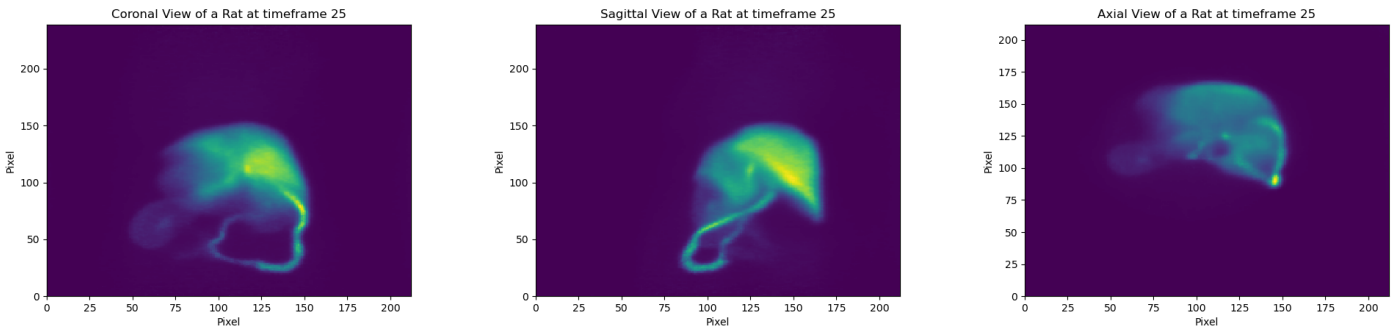


Figure: Three views for a dynamic acquisition on a rat

References

1. Canny, J. A *Computational Approach to Edge Detection*. IEEE Transactions on Pattern Analysis and Machine Intelligence 8(6). 1986.
2. Diaz, A.M.A. et al. *Evaluation of the High Affinity of [18F]fluoropyridine- candesartan in rats for PET imaging of renal AT1 receptors*. Nuclear Medicine and Biology, 96-7. 2021.
3. Fahey, F. et al. *Variability in PET quantitation within a multicenter consortium*. Med. Phys. 37(7). 2010.
4. Hatt, M. *Classification and evaluation strategies of auto-segmentation approaches for PET: Report of AAPM Task Group No. 211*. Med. Phys. 44(6). 2017.
5. Meikle, S.R. et al. *Quantitative PET in the 2020s: A Roadmap*. Phys. Med. Biol. in press. 2020.

Manual Segmentations: Why Not

- The image for a given timeframe is not necessarily very different from the subsequent one;
- The shape is not always nice and solid;
- The model requires the whole volume to be segmented;
- There is a high risk for inter- and intra-user variability.

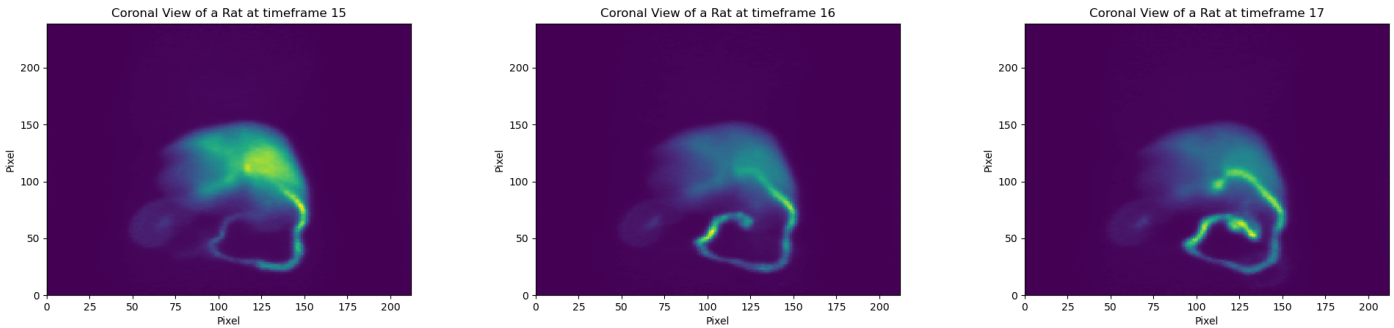
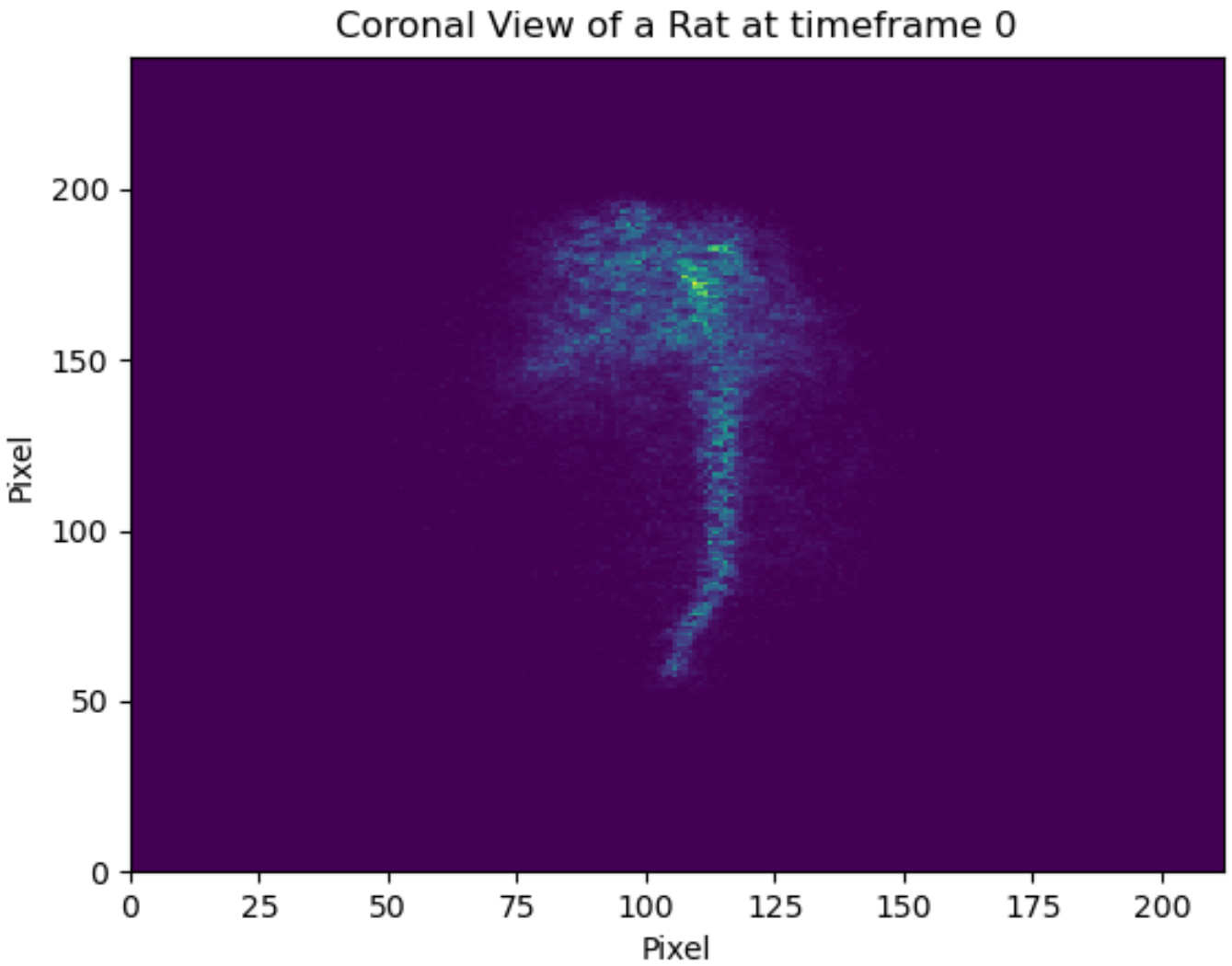


Figure: Three temporally adjacent timeframes for a given phantom acquisition

Manual Segmentations: Why Not



Selection of the Segmentations

- Some segmentations were not kept for the analyses;
  - It was too early in the acquisition;
  - The visual segmentation was aberrant.

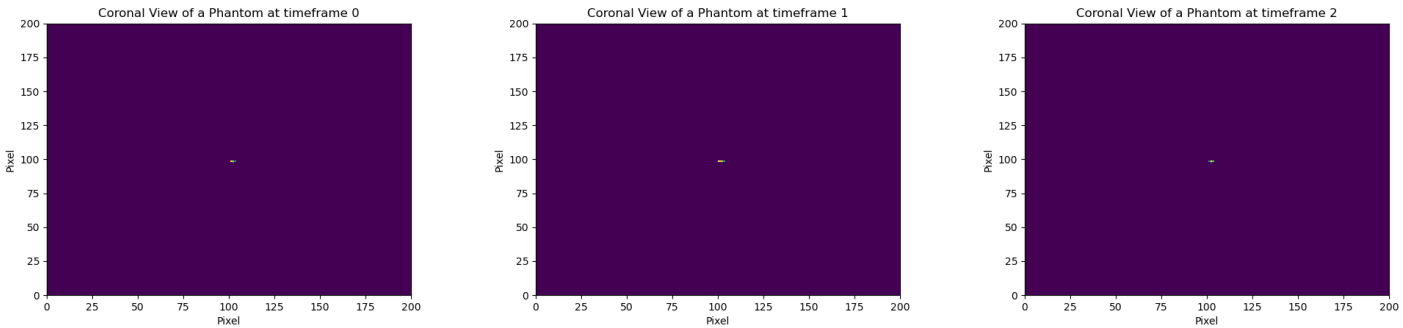


Figure: Some segmentations that were not kept for the subsequent analyses