Cerenkov Imaging as a Tool for PET Radiotracer Synthesis on the EWOD Microfluidic Platform

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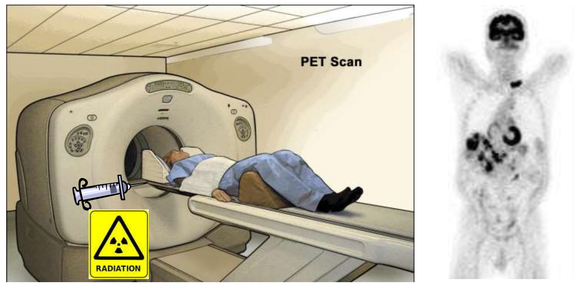
INTRODUCTION

Positron Emission Tomography (PET) is an imaging modality that uses a positron emitting radioactive compound (radiotracer, probe) to image a molecular process.



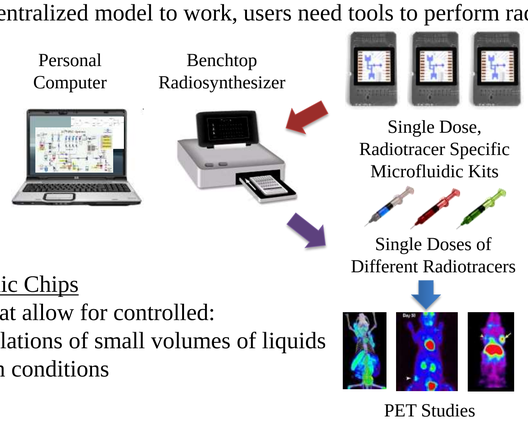
PET radiotracer production will benefit from a shift in paradigm.

Centralized Model: Produce radioisotope → Synthesize radiotracer → Distribute → Image

Decentralized Model: Produce radioisotope → Distribute → Synthesize radiotracer → Image

The decentralized model will give clinicians/researchers the ability to synthesize for research or for the clinic new radiotracers without negotiations with a radiopharmacy.

For the decentralized model to work, users need tools to perform radiotracer synthesis.

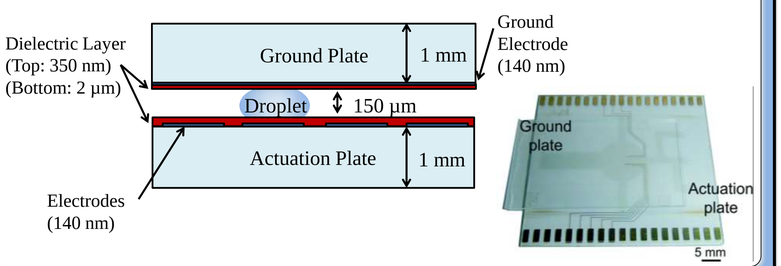


Microfluidic Chips

Devices that allow for controlled:

1. manipulations of small volumes of liquids
2. reaction conditions

Electrowetting on dielectric (EWOD) is a promising microfluidic platform for [^{18}F]fluoride radiotracer synthesis.



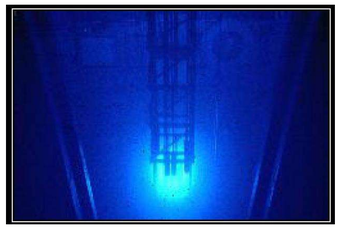
Optimization tools are very important when developing a new technology.

Is quantitative imaging of ^{18}F on a microfluidic chip possible/practical?

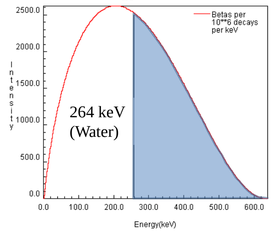
SYSTEM DESIGN

As previous work confirmed the generation of Cerenkov radiation on a microfluidic chip, we have developed a detection system based on Cerenkov emission.

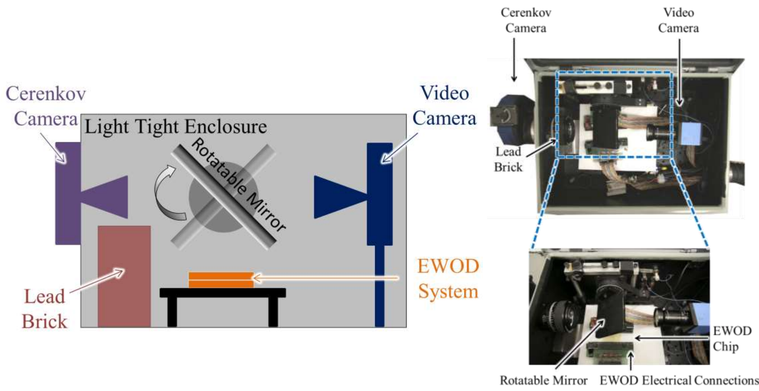
Cerenkov radiation describes photons predominantly in the UV and visible spectrum produced when a particle travels faster than the speed of light in the surrounding medium.



Positron Energy Distribution for ^{18}F



We designed a two optical camera setup integrated into a light tight enclosure.

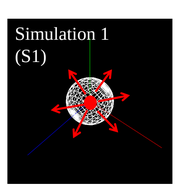


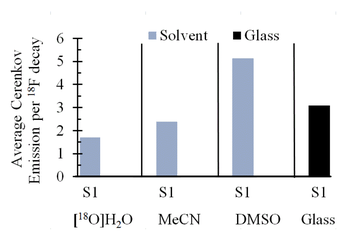
SIMULATION

Material properties affect Cerenkov photon yield.

Material	Index of refraction, n	Density, ρ [g cm^{-3}]
[^{18}O]H_2O	1.33	1.10
Acetonitrile (MeCN)	1.34	0.79
Dimethyl Sulfoxide (DMSO)	1.48	1.10
Glass	1.52	2.53

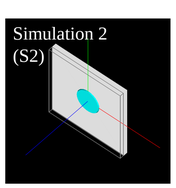
Geant4 Simulation

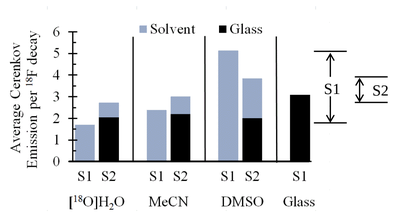




Cerenkov photons triple from [^{18}O]H_2O to DMSO

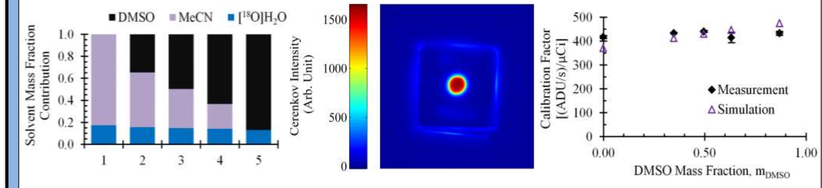
The planar geometry of EWOD may work to our advantage.





VALIDATION OF SIMULATION

Measurements validate independence of calibration factor with droplet composition.



SAMPLE STUDY

We find good agreement between radioactivity measured with a dose calibrator and Cerenkov imaging...

1. After 1st [^{18}F] load

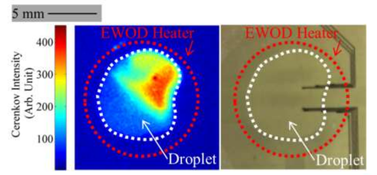
2. After 2nd [^{18}F] load

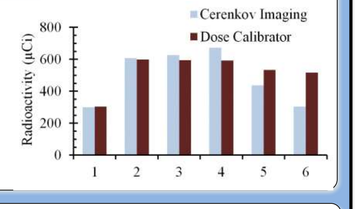
3. After evaporating solvent (dose calibrator) then adding MeCN (Cerenkov)

4. After MeCN evaporation (dose calibrator) then adding precursor solution (Cerenkov)

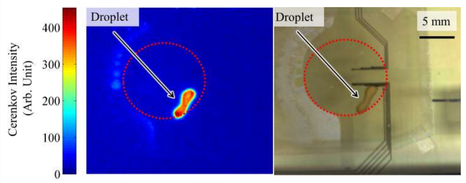
5. After fluorination reaction (dose calibrator) then adding HCl/MeCN solution (Cerenkov).

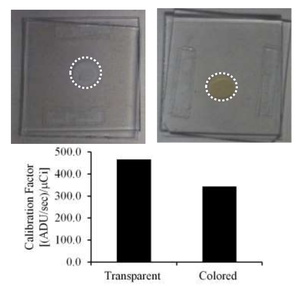
6. After hydrolysis reaction.



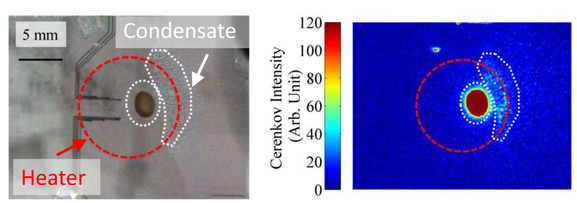


...except when the droplet becomes stained.





Observations from Cerenkov images enable optimization of the mixing protocol that improves radiochemical yield from 50 ± 3% (n = 3) to 72 ± 13% (n = 5).



CONCLUSION

- We developed a Cerenkov/real-time imaging system for PET radiotracer synthesis on EWOD.
- Cerenkov imaging quantitation was simulated and verified with measurements.
- Qualitative studies enabled an overall increase in the radiochemical yield from 50±3% (n=3) to 72±13% (n=5).

References: Dooraghi et al. *Analyst* 2013; Chen et al. *Lab Chip* 2014