High-Z plastic scintillators for a total-body SPECT detection system: the reSPECT project

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PRIN: PROGETTI DI RICERCA DI RILEVANTE INTERESSE NAZIONALE
Bando 2022 Prot. 2022Z72Y3K

Finanziato dall'Unione europea NextGenerationEU

Ministero della Salute

Italiadomani
PIANO NAZIONALE DI RIPRESA E RESILIENZA

Ministero dell'Università e della Ricerca

The reSPECT project

The goal of the reSPECT project is improving the performances of the SPECT detectors in use today by designing a new detection system based on plastic scintillators doped with high-Z impurities, with the possibility to realize a total-body SPECT.

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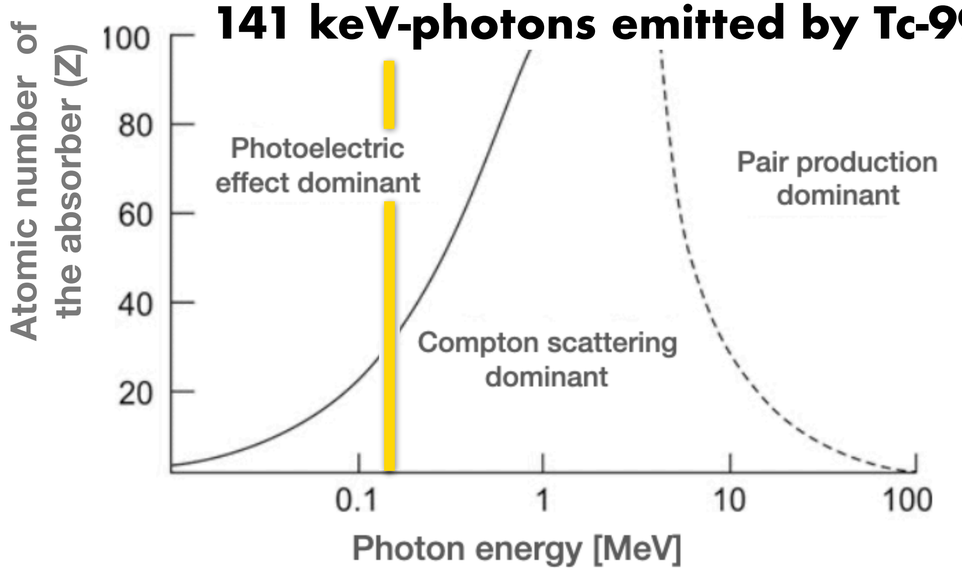
The most used radionuclide for SPECT exams is Technetium-99 metastable, that emits 141 keV γ-rays ($\tau_{1/2} \approx 6$ h).

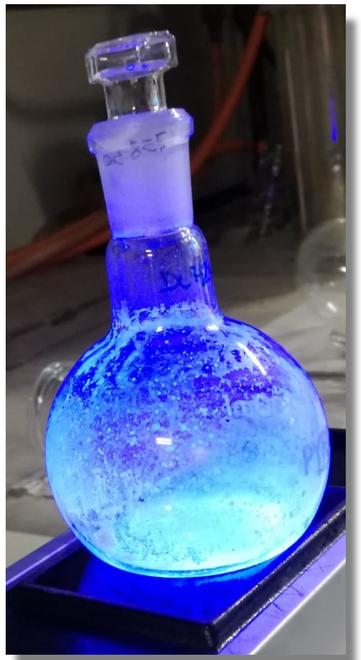
141 keV-photons emitted by Tc-99m

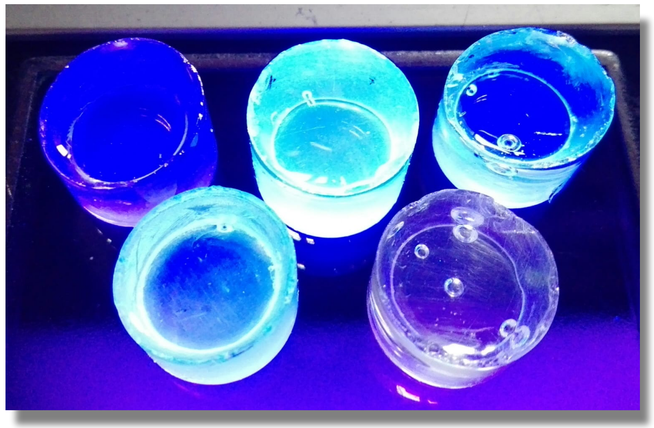


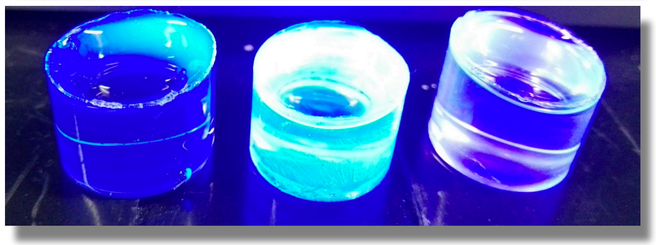
To reduce the discharge of "good" events, the probability of photoelectric absorption inside the scintillator must be maximized. Typically, inorganic scintillators are exploited due to their high atomic number.

High-Z doped plastic scintillators

- Exploit plastic scintillators since they are extremely fast, light, inexpensive and easy to shape.
- Increase the atomic number by enriching them with high-Z impurities.







High-Z doped plastic scintillators

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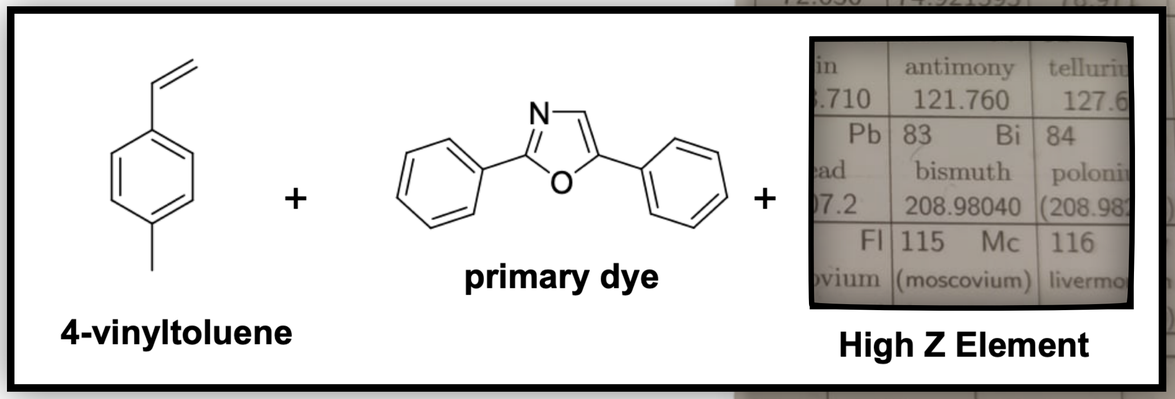
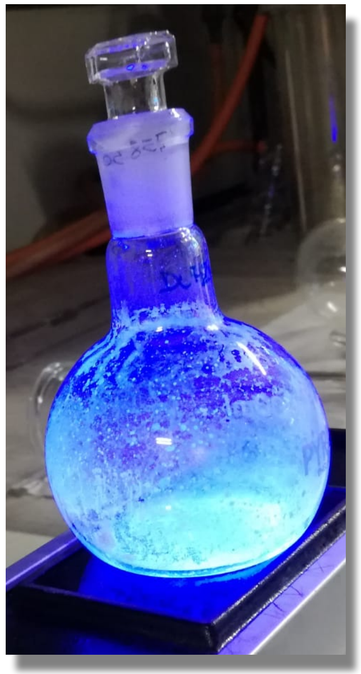
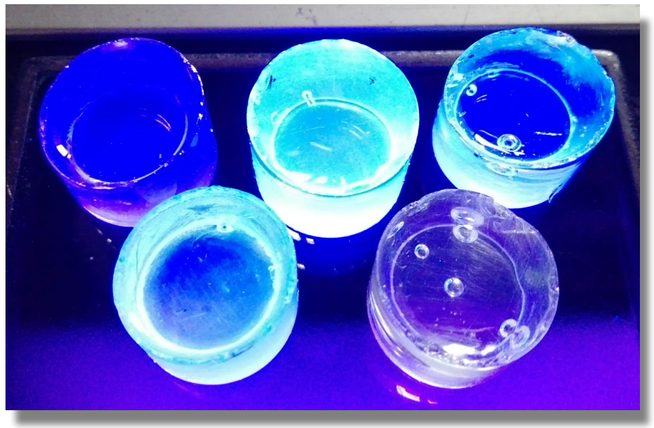
INFN CENTRO RICERCHE ENRICOFERMI

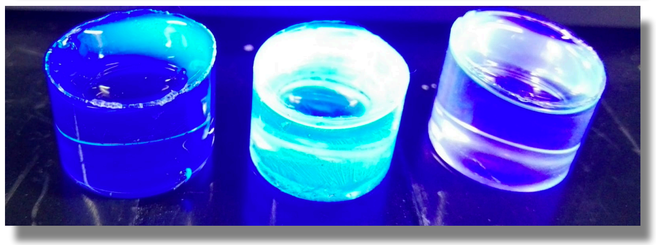
- Exploit plastic scintillators since they are extremely fast, light, inexpensive and easy to shape.
- Increase the atomic number by enriching them with high-Z impurities.

^{53}I	^{58}Ce	^{64}Gd	**^{68}Er**	^{81}Tl	^{82}Pb	**^{83}Bi**



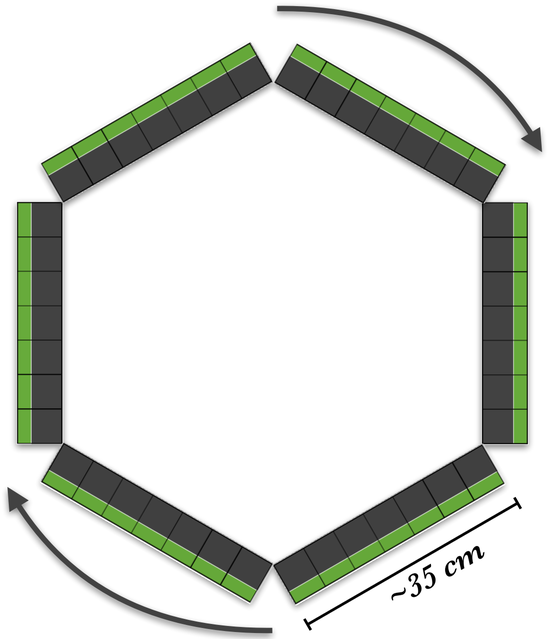






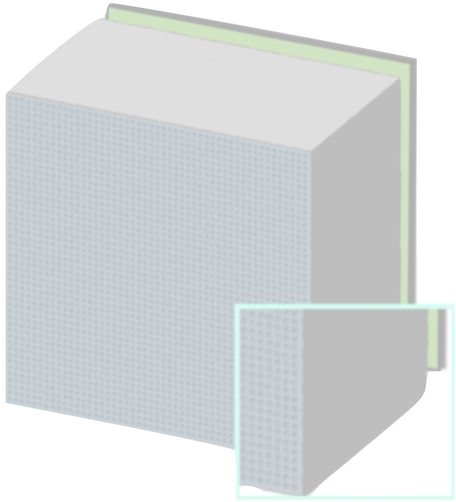
Scintillators with dopant concentrations higher than 10% are not available on the market. BUT we can produce them in our laboratory, so ... let's play magic!

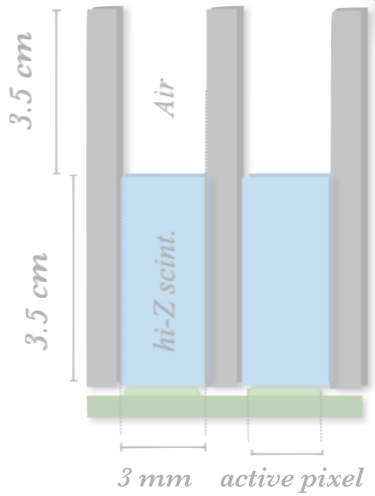
The reSPECT detection system



Modular structure that will be able to revolve around the patient, enabling multi-angle data acquisition.

Each module will consist of a 3D-printed **tungsten frame** that serves both as a collimator and as a container of the **scintillator segments**, polymerized directly inside the holes.





Readout performed by **Silicon-based photodetectors** arranged in small-size pixels, individually coupled to the scintillator segments.

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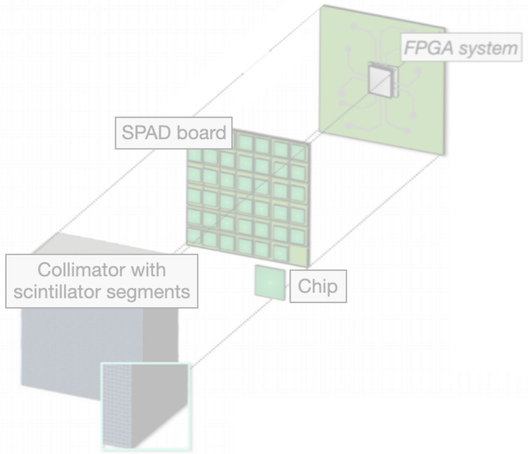

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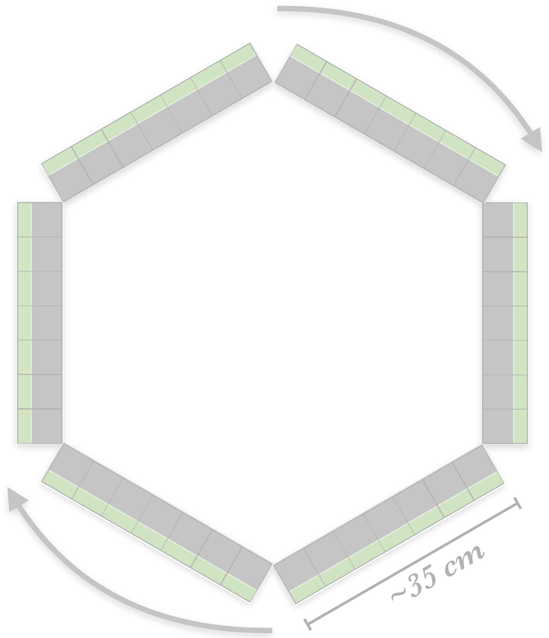

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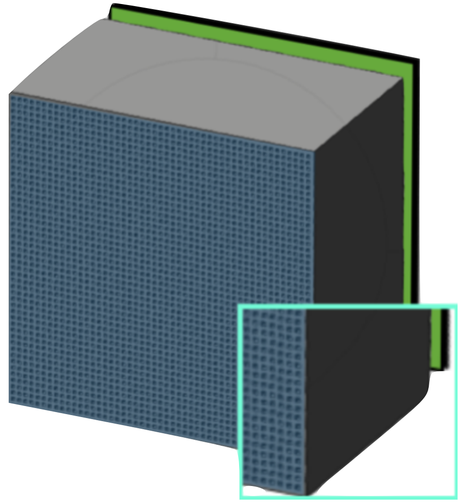

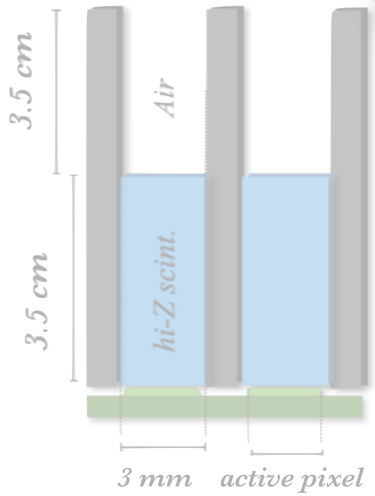

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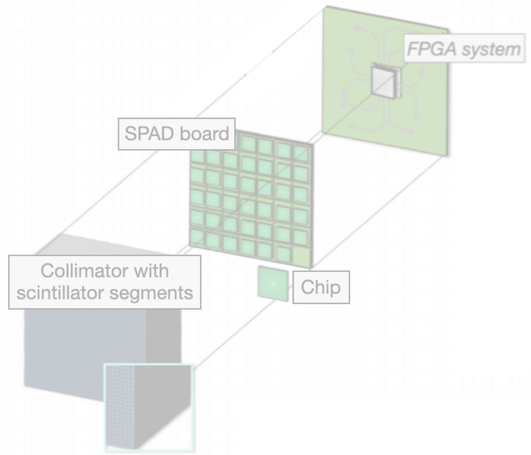

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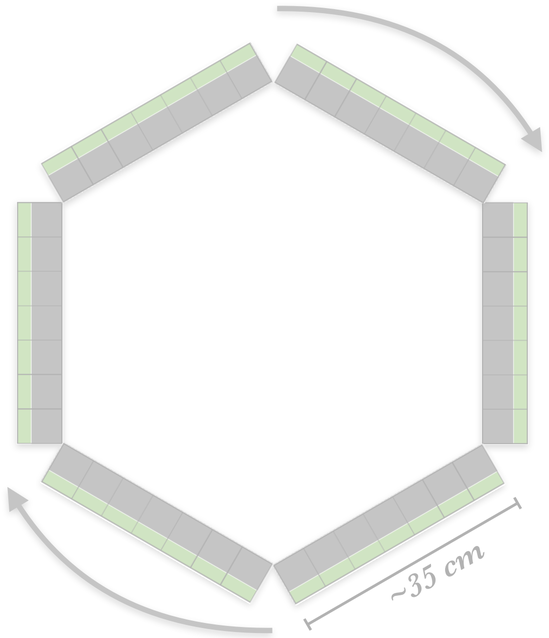

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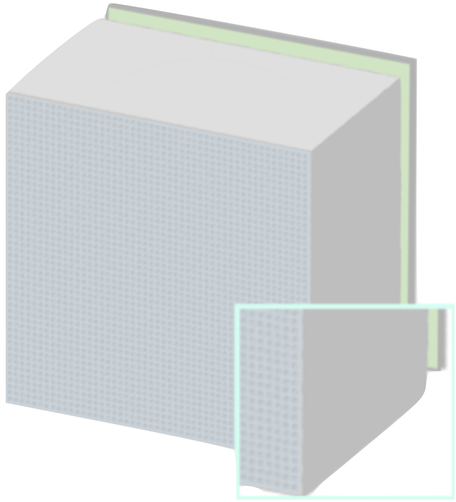

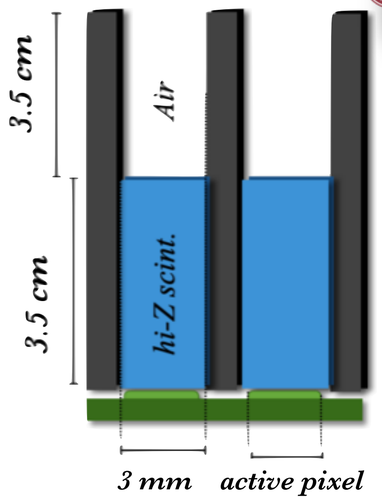

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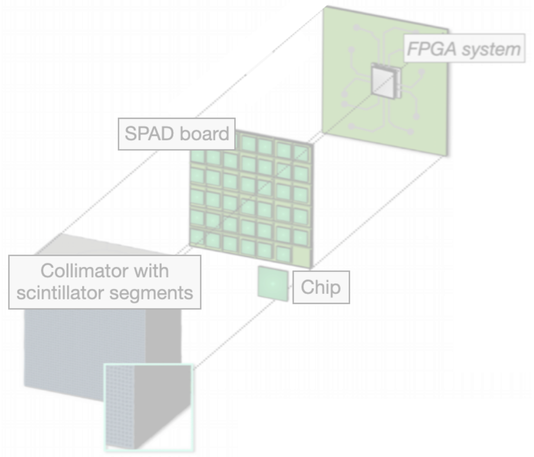

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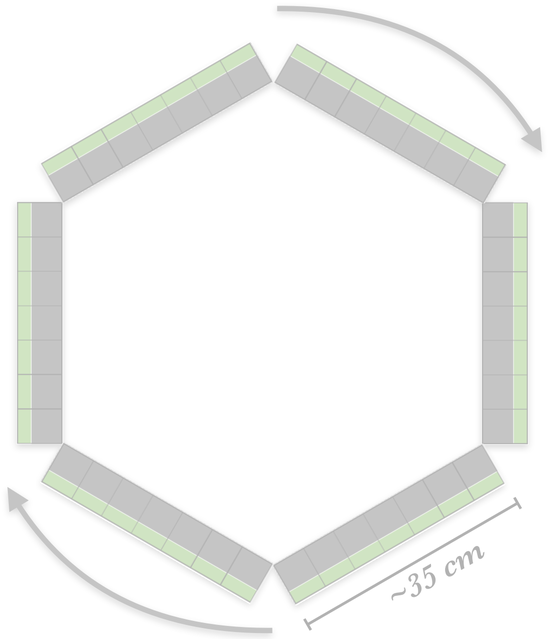

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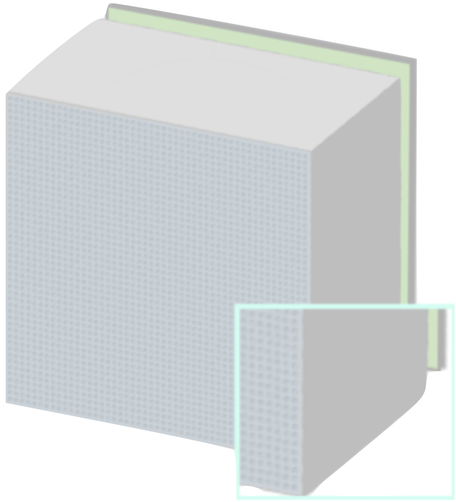

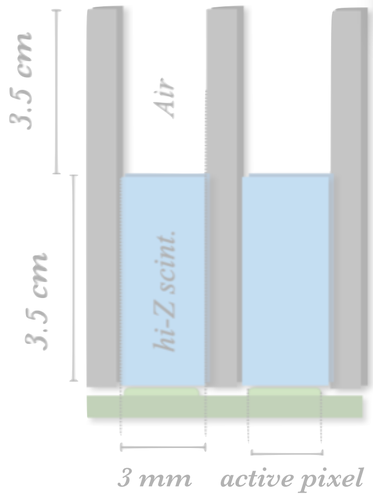

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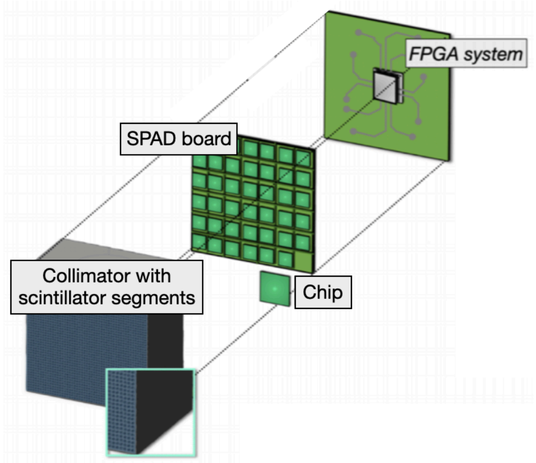

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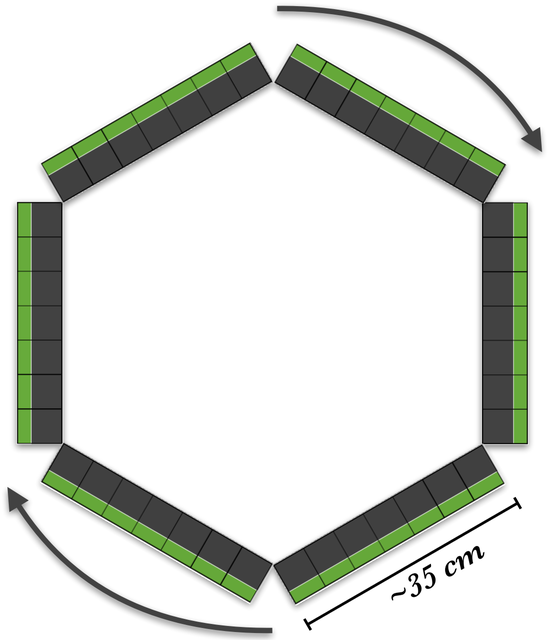

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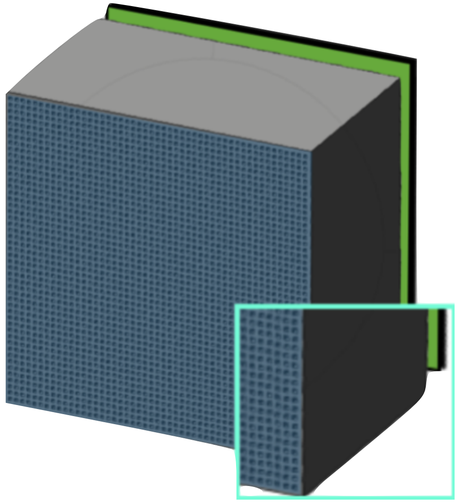

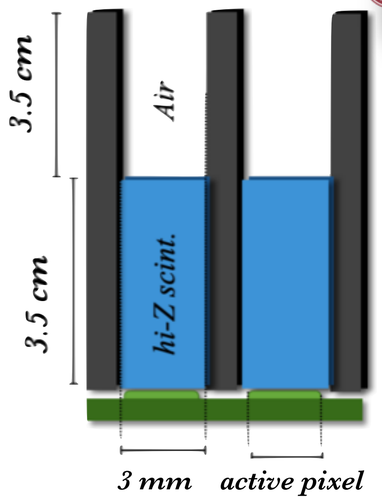

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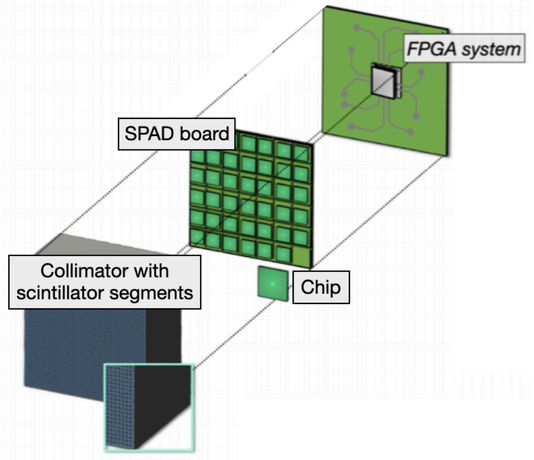
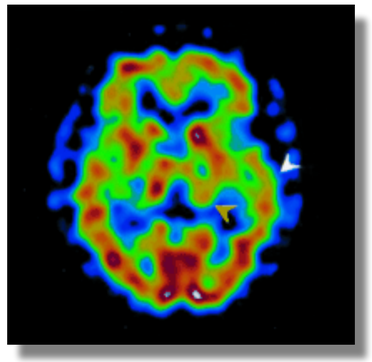


The granularity of the active material is crucial:
in order to ensure a good space resolution, the same pixel size has been maintained for the readout.

Expected performances



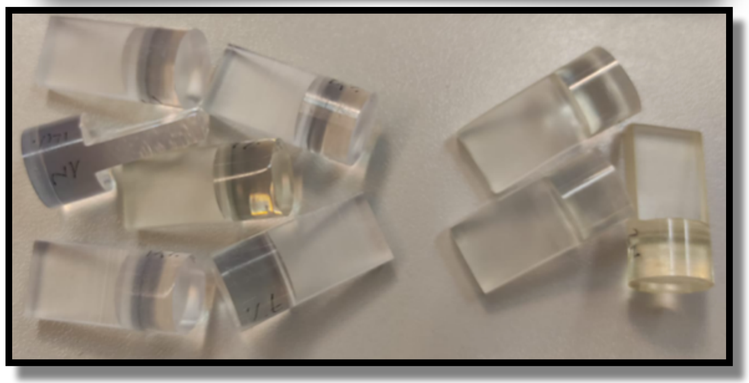
- The expected performances of the reSPECT detection system have been obtained through MC simulations
- The simulated scintillators have a Bismuth concentration of 10%

- ✓ Low cost
- ✓ Compliance with MRI and theranostic studies
- ✓ Possibility to conceive a total-body SPECT thanks to the modular structure
- ✓ Unparalleled counting rate capability

SPECT DETECTION SYSTEM	SENSITIVITY PER MODULE @140 keV [cpm/μCi]	SYSTEM SPATIAL RESOLUTION (FWHM) @10 cm [mm]	DECAY TIME [ns]	RATE CAPABILITY [cps/cm^2]	TOTAL COST –	MAGNETIC RESONANCE IMAGING COMPLIANCE	RADIOMETABOLIC DOSIMETRY COMPLIANCE
Anger Camera (NaI) FoV: 53 x 39 cm^2	170	7.4	250	0.25k-3k	$$	✗	✗
CZT FoV: 39 x 51 cm^2	190	7.6	350	30k-700k	$$$	✓	✗
reSPECT 6 rotating blocks, FoV: 35 x 35 cm^2	**184** (Energy cut 80 keV)	**8.9** (For pixel size: 2 mm)	**2-5**	**50M-200M**	**$**	✓	✓

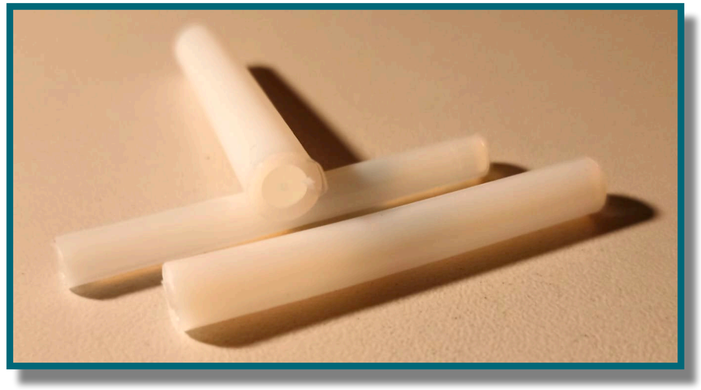
New organic scintillating molecules

- We synthesized and patented [1] several new organic scintillating molecules containing aromatic fragments.
- We produced plastic scintillators embedding our scintillating molecules in a polyvinyl-tuoluene (PVT) matrix, in order to chose the best candidate to create the Bismuth-doped samples ("2N").
- We are producing samples of high-Z organic scintillators with different sizes, shapes and composition.
- Transparency results to be good up to very high concentrations.
- We are testing them with different radioactive sources and readout systems.

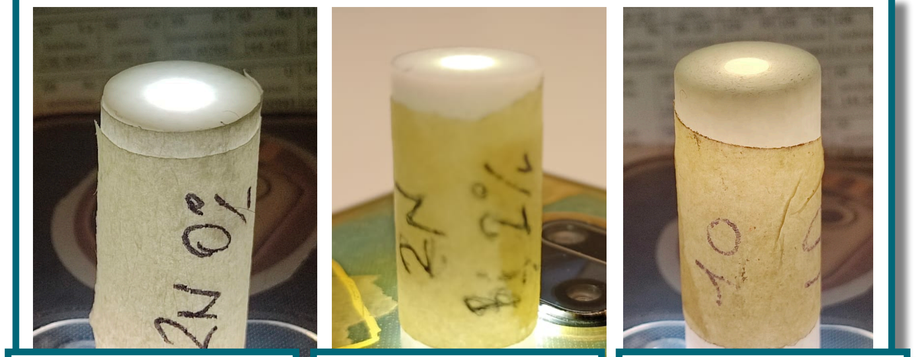


[1] Mattiello L.; Patera V.; Belardini A.; Rocco D.; Marafini M.; Organic Scintillator. *Patent* WO2023156957A1, 2023.

The addition of Bismuth does not deteriorate the time resolution!

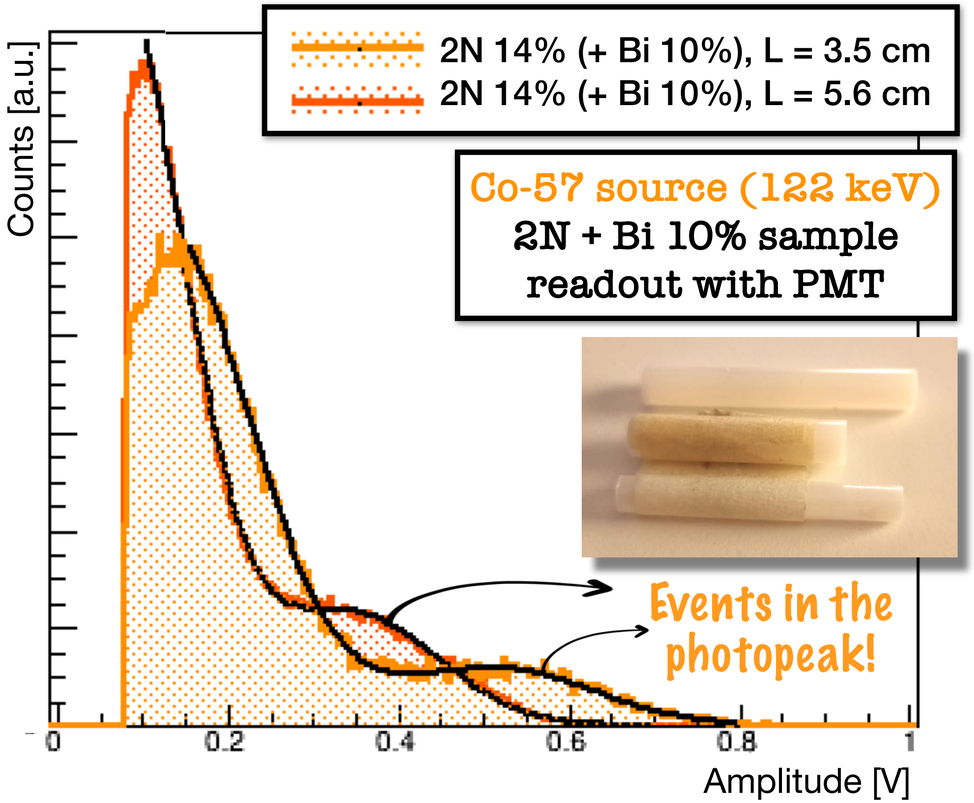


In order to improve the collection efficiency of the scintillation light, we produced samples where the polymerization process happens directly inside a PTFE (teflon) coating.



PVT + 2N(14%) + Bi(0%) | PVT + 2N(14%) + Bi(2%) | PVT + 2N(14%) + Bi(10%)

High-Z doped scintillator prototypes: performances



Scintillator	Light Output [a.u.]
2N + 0% Bi	100%
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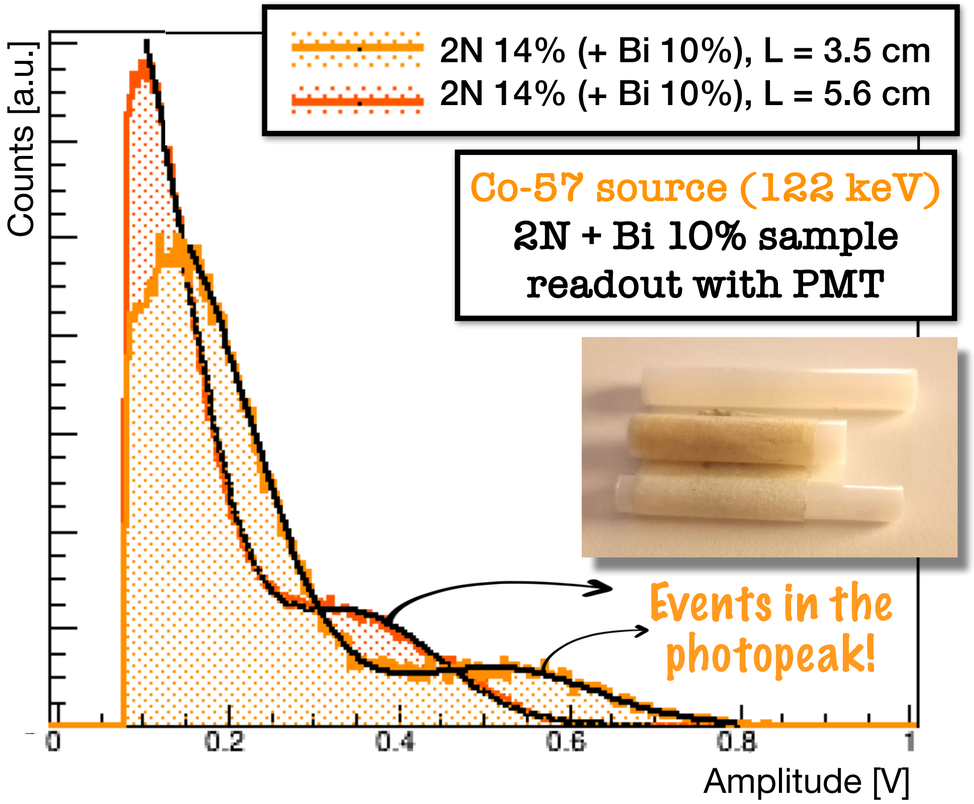

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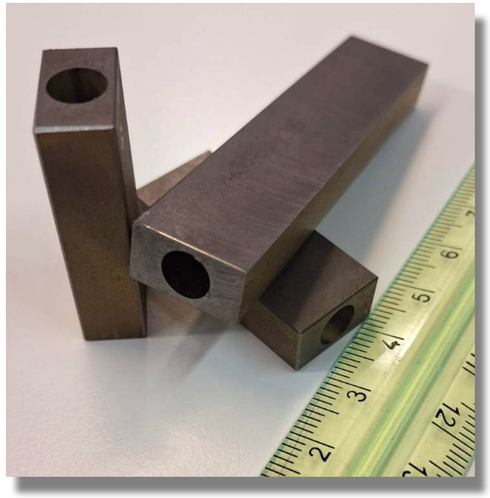
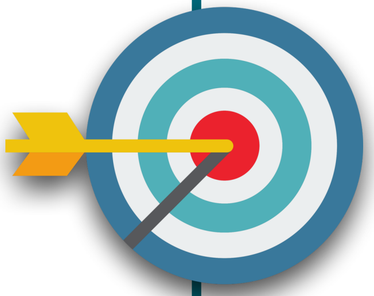
- ☑ With the reSPECT project, we are targeting a **total body SPECT**, accessible to the National Health System in terms of cost, space and diagnostic efficiency.
- ☑ We produced **10%-doped samples** obtaining promising results.
- ☑ We managed to detect the **photoelectric peak** with an energy close to that of Tc-99m.



To do:

- ☐ Tests with samples containing other high-Z dopants (e.g. Erbium) and higher concentrations.
- ☐ Data acquisitions with Technetium-99 metastable.
- ☐ Polymerization of the samples inside the Tungsten hive.

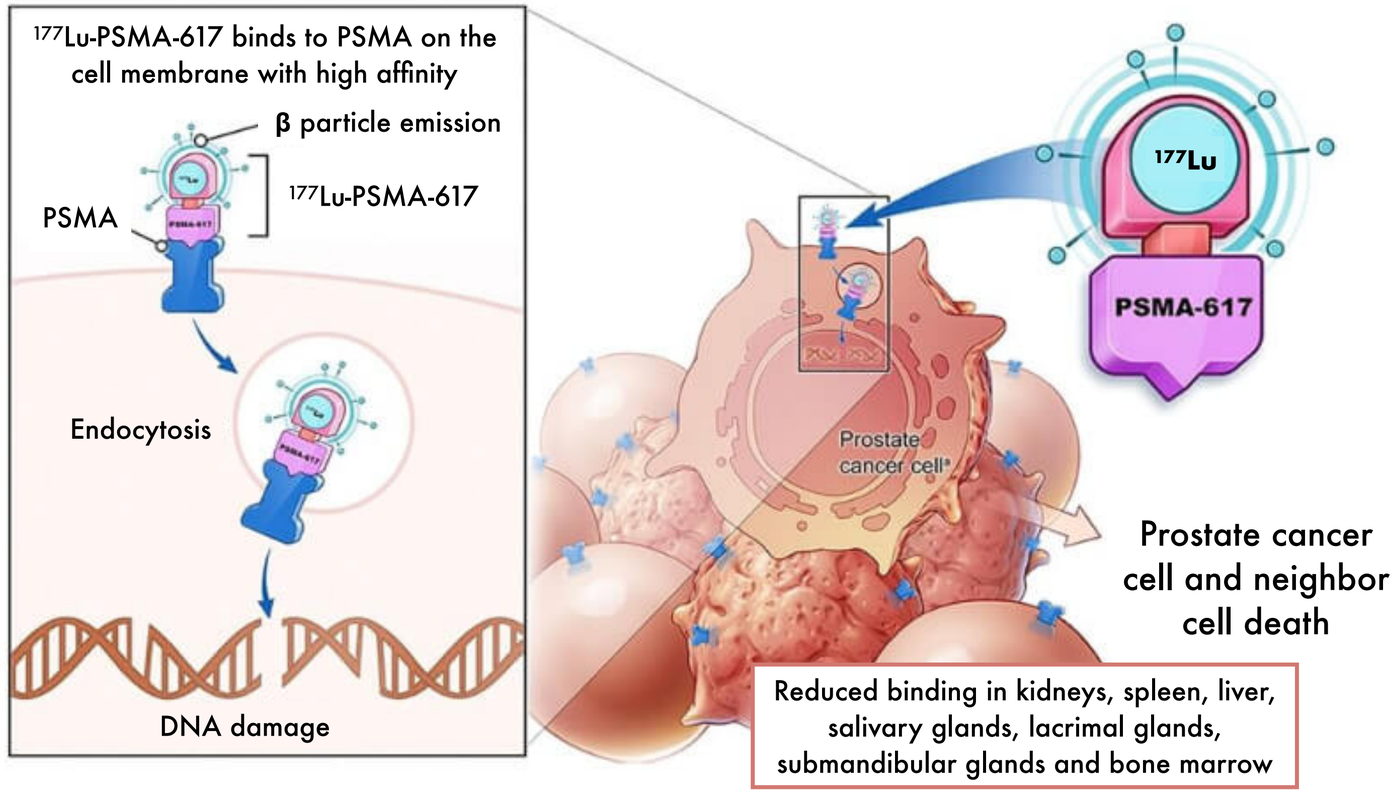
TRONDHEIM: SPECT for prostate cancer treated with 177-Lutetium



The goal of this project is the development of a portable γ-rays detector, based on high-Z doped plastic scintillators, in order to improve the overall survival of prostate cancer patients treated with ^{177}Lu-PSMA-617 by customizing their treatment.

^{177}Lu-PSMA-617 treatment for mCRPC

- To date, the most effective treatment for metastatic Castration Resistant Prostate Cancer (mCRPC) is ^{177}Lu-PSMA -617 radiometabolic therapy.
- Thanks to the presence of the PSMA protein, the radiopharmaceutical molecules mainly link to the tumor cells, that are damaged by the electrons emitted by ^{177}Lu via β- decay (maximum tissue penetration = 2 mm).
- ^{177}Lu also emits 208 keV gamma rays, allowing for dosimetric studies by means of a SPECT detector.
- ^{177}Lu half-life = 6.7 days



Personalized dosimetry for treatment optimization

- To date, in the clinical practice all the patients receive the same radiopharmaceutical activity.
- This leads to a systematic under treatment.
- By determining the rates of radiopharmaceutical **uptake and clearance** of each patient, it is possible to customize the treatment.

✓ reduction of the toxicity
✓ improvement of the therapeutic effectiveness

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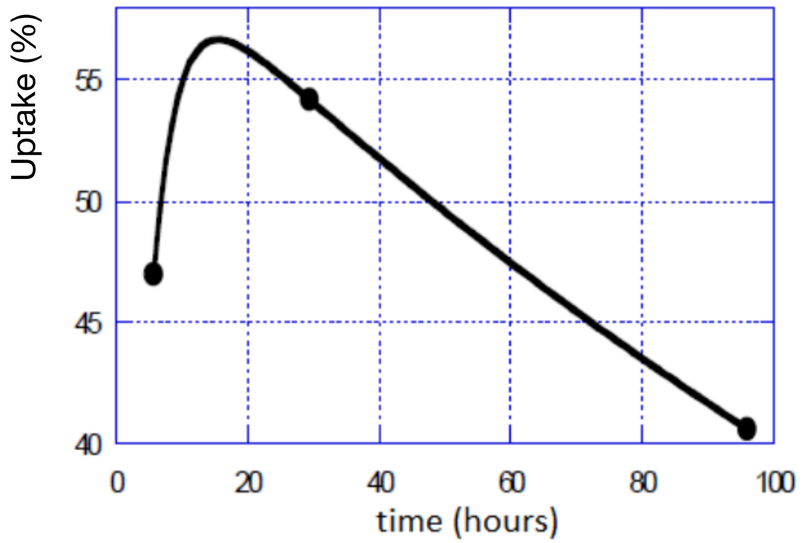
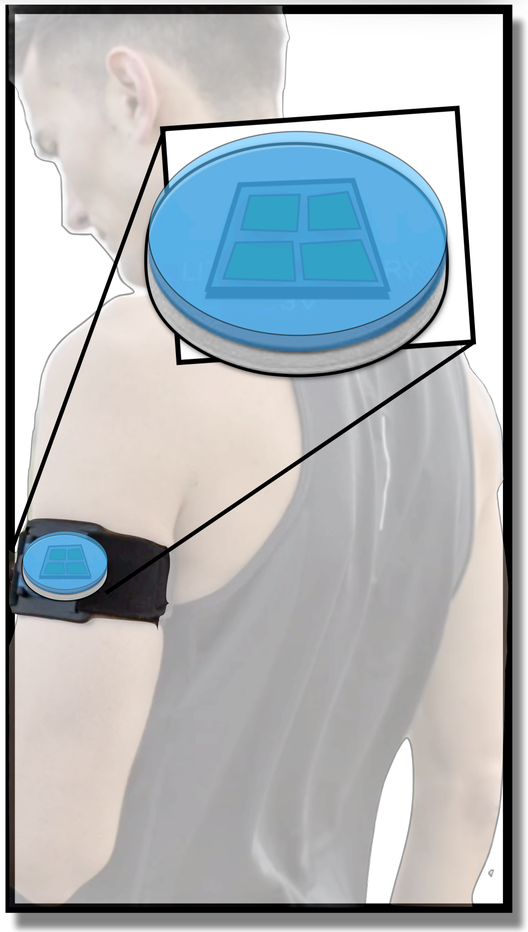


Portable γ-rays detector to retrieve the activity-vs-time curve for each patient after the administration of a reference (low) dose → determination of the radiopharmaceutical biokinetics



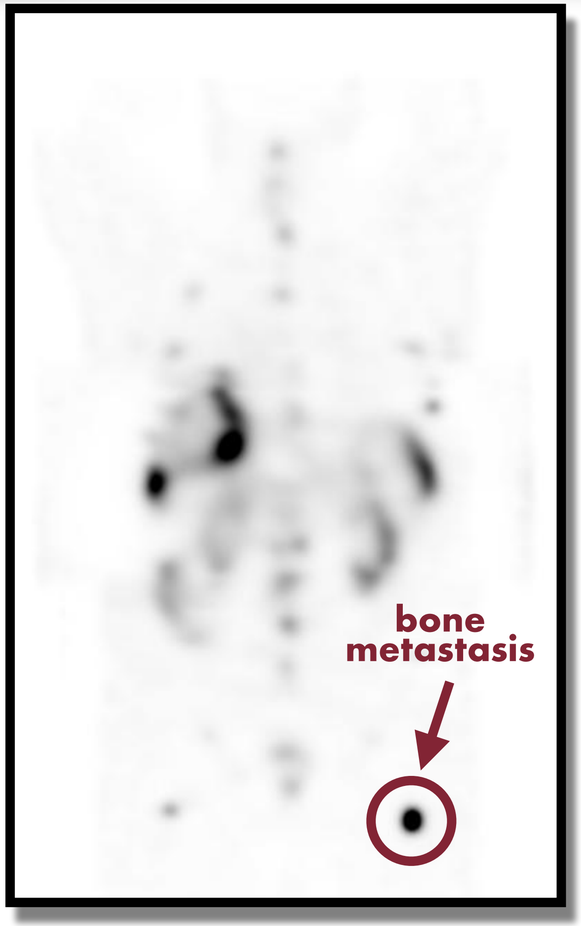
The TRONDHEIM project

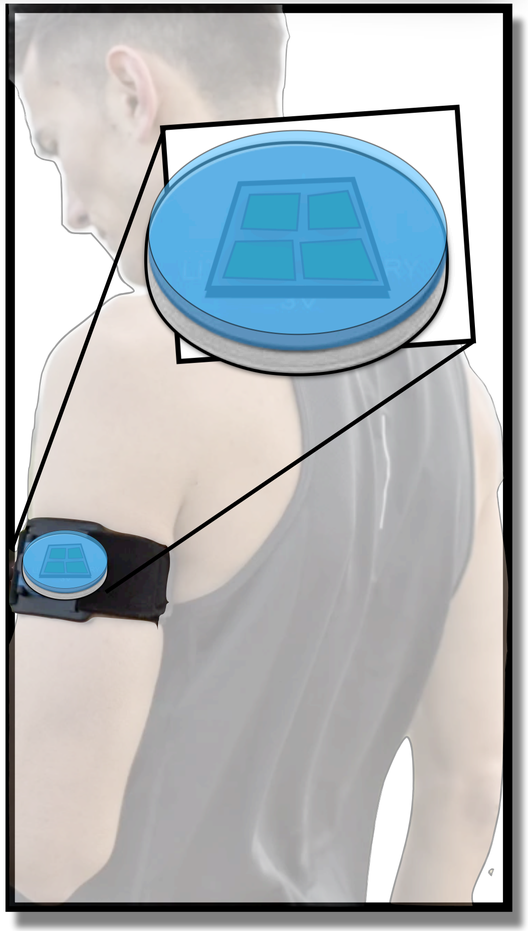
The TRONDHEIM γ-rays detector:

- ➡ Plastic scintillators enriched with high-Z elements
- ➡ Silicon-based integrated readout system with FPGA modules

- ✓ Light and compact device
- ✓ Low cost
- ✓ High counting rate capability

- **Electronics development**
- **High-Z plastic scintillators production**
- **How many devices? Where should the patient wear them?**





come fai..SBAI

Grazie per l'attenzione!

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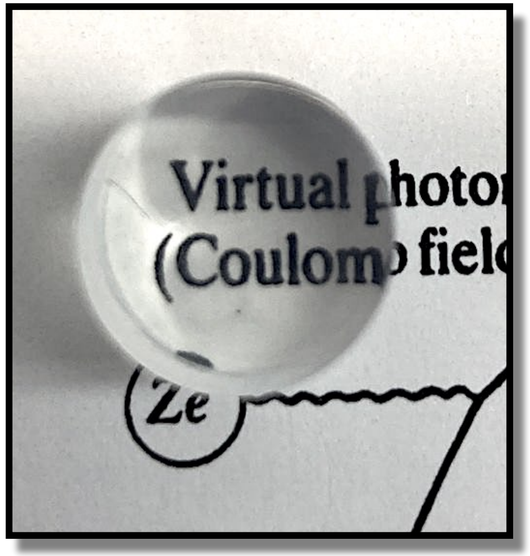


Alberto Burattini, Marta David, Angelica De Gregorio, Giuseppe De Vincentis, Gaia Franciosini, Viviana Frantellizzi, Marco Garbini, Leonardo Gasparini, Nils Krah, Marco Magi, Michela Marafini, Leonardo Mattiello, Annalisa Muscato, Roberto Passerone, Vincenzo Patera, Flaminia Quattrini, Daniele Rocco, Alessio Sarti, Angelo Schiavi, Marco Toppi, Giacomo Traini

Spare slides

Single-photon emission computed tomography

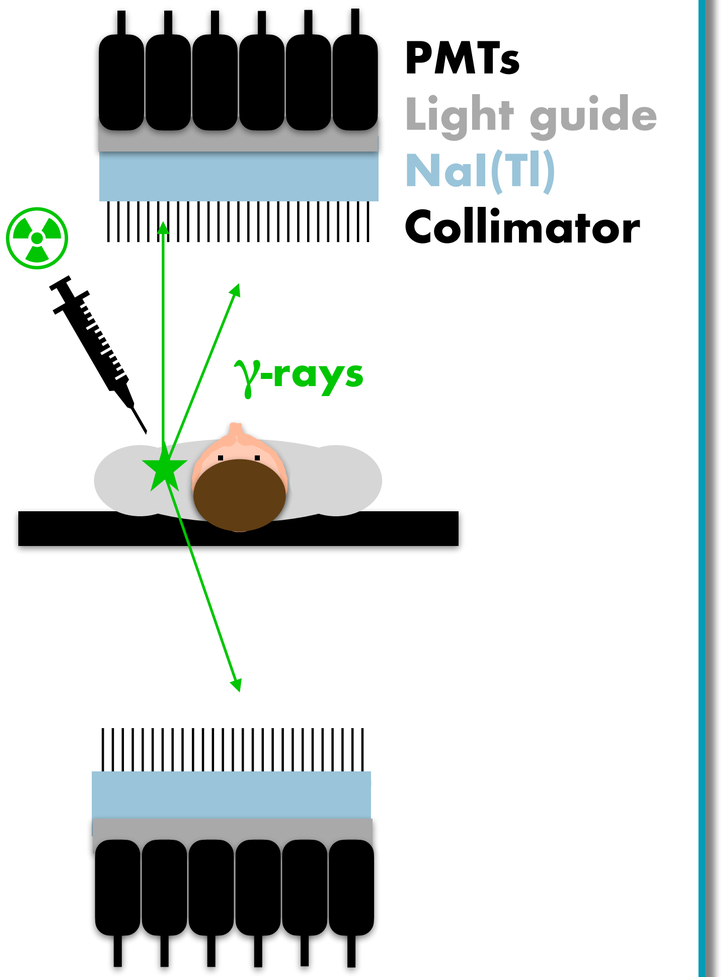
- Nuclear imaging technique that allows to investigate the patient's physiological processes.
- Essential tool for cancer detection and several other diagnoses.
- In Italy, SPECT scans are more widespread than PET scans! [1]
- Typically, the detection of the gamma rays is carried out by the Anger Camera.

1. Radiopharmaceutical production
2. Administration of the radiopharmaceutical
3. Data acquisition (gamma rays detection)
4. Tomographic image reconstruction
5. Image analysis (diagnosis)

[1] https://www.dati.salute.gov.it/dati/dettaglioDataset.jsp?menu=dati&idPag=80

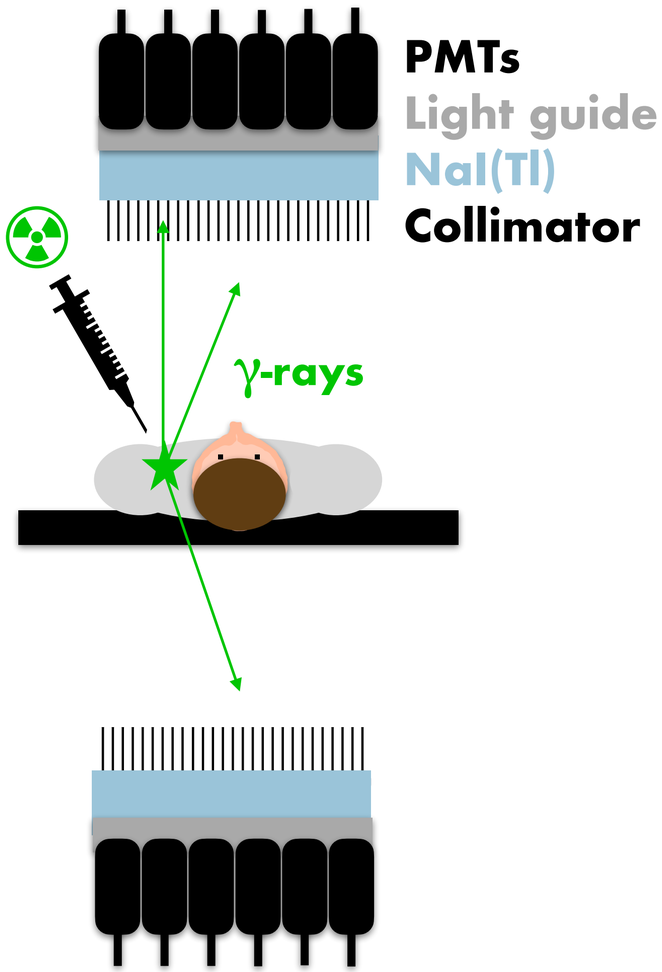
Single-photon emission computed tomography

Anger camera



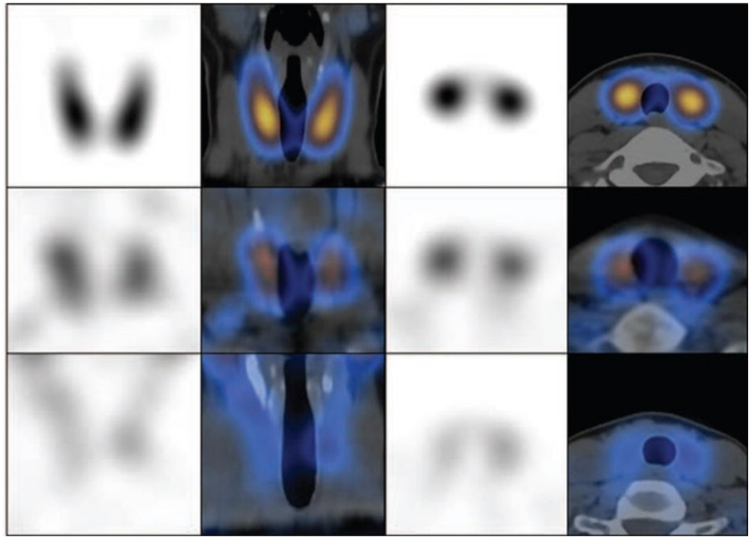
Single-photon emission computed tomography

Anger camera



Thyroid SPECT/CT

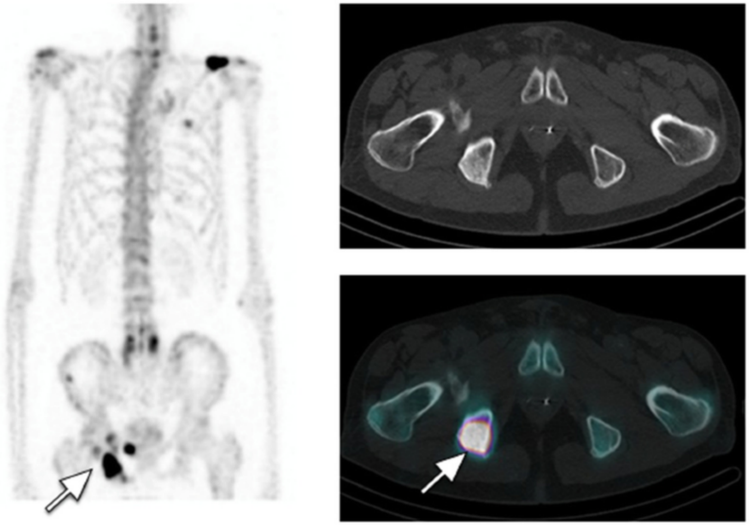
Example: detection of Graves' disease, euthyroid and thyroiditis



http://dx.doi.org/10.1097/MD.0000000000004170

Bone SPECT/CT

Example: osteoblastic lesions detection

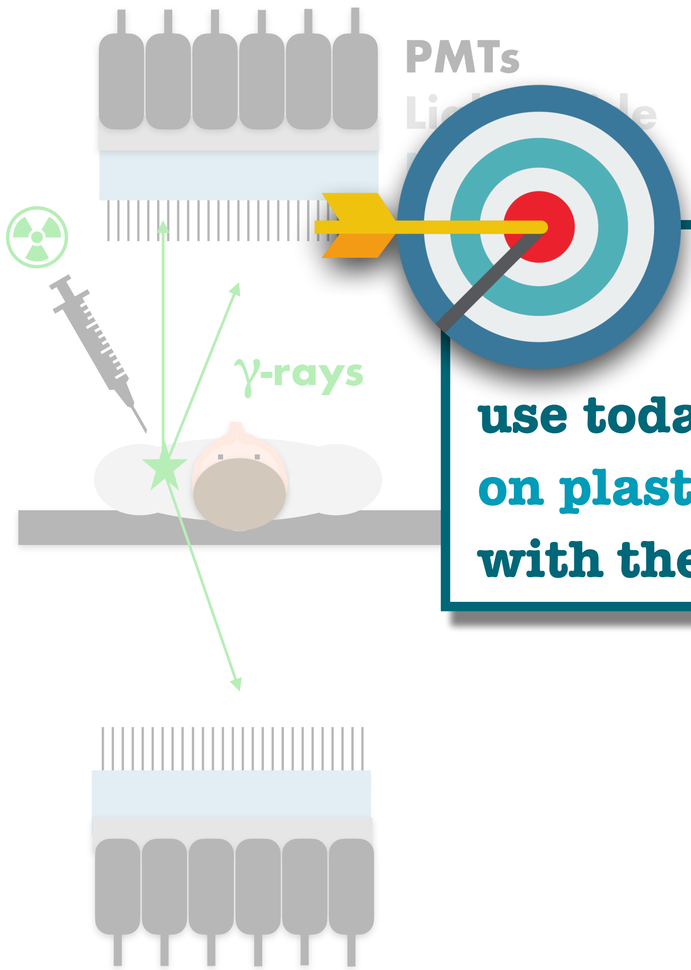


https://doi.org/10.1186/s40644-020-00333-y

The widespread diffusion of SPECT scans is mainly due to the high number and availability of γ-emitting radiotracers. But to date, SPECT scans have worse performances than PET scans in terms of resolution.

Single-photon emission computed tomography

Anger camera



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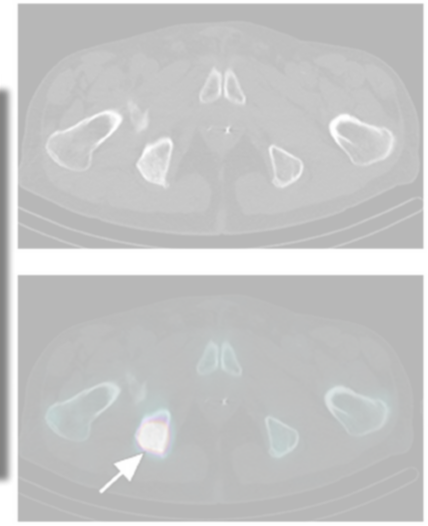


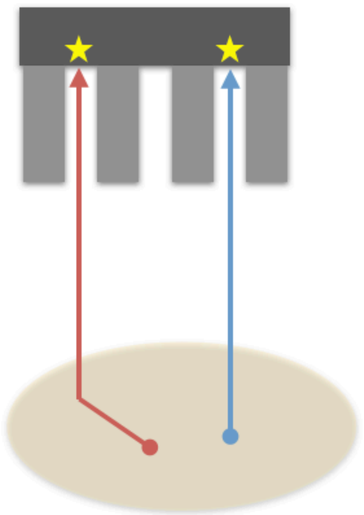
https://doi.org/10.1186/s40644-020-00333-y

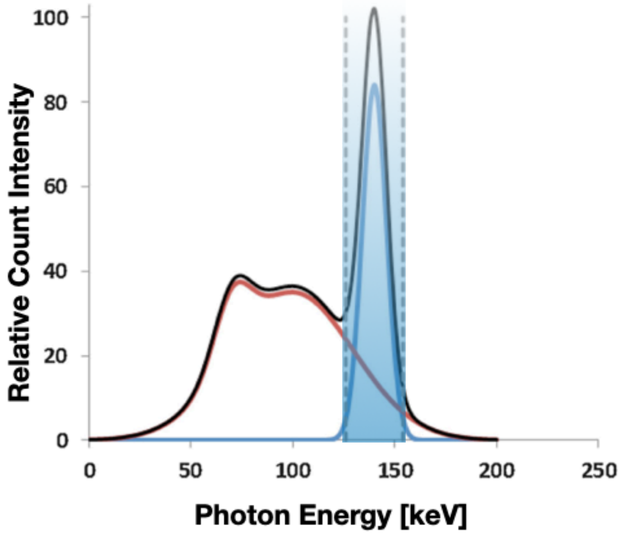
The goal of the reSPECT project is improving the performances of the SPECT scanners in use today by designing a new detection system based on plastic scintillators doped with high-Z impurities, with the possibility to realize a total-body SPECT.

The widespread diffusion of SPECT scans is mainly due to the high number and availability of γ-emitting radiotracers. But to date, SPECT scans have worse performances than PET scans in terms of resolution.

The role of photoelectric absorption in SPECT exams

The most used radionuclide for SPECT exams is Technetium-99 metastable, that emits 141 keV γ-rays ($\tau_{1/2} \approx 6$ h).





Tc-99m photopeak: these events carry the correct information about the radiopharmaceutical position.

Scattered photons: these events must be rejected to exclude the photons that changed direction inside the patient.

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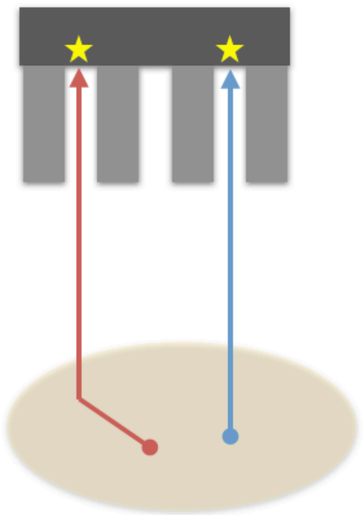

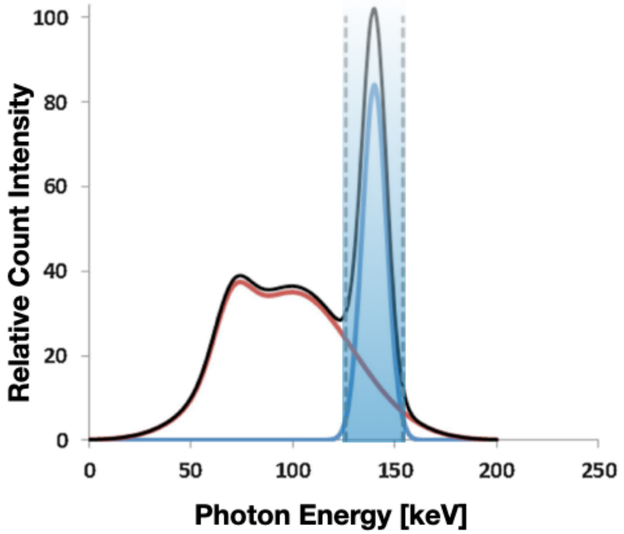

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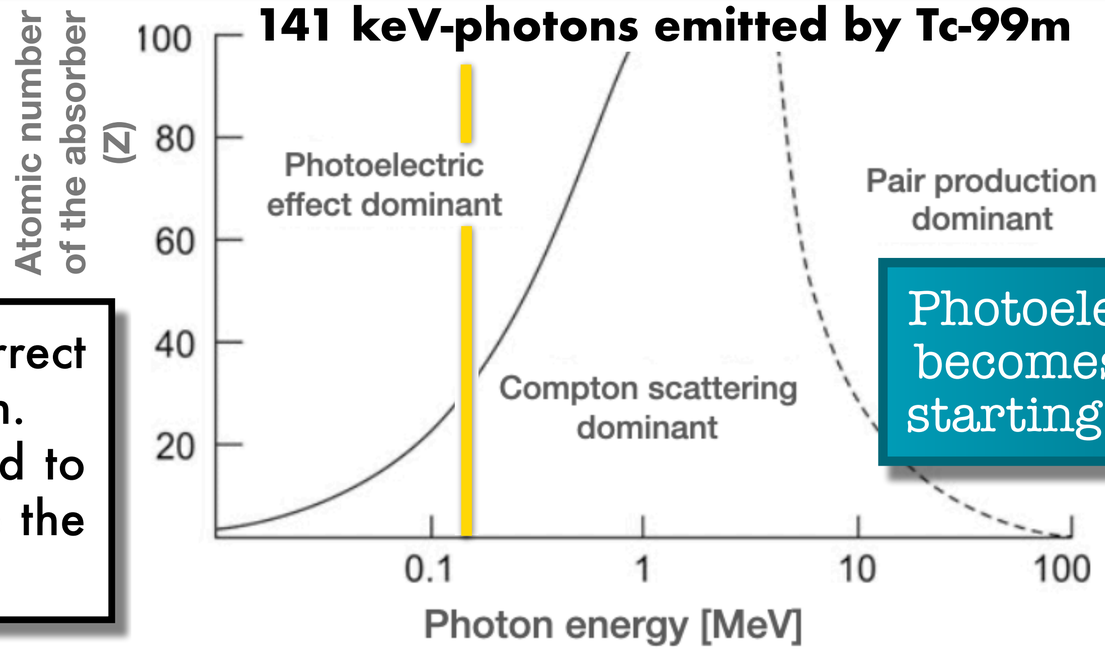
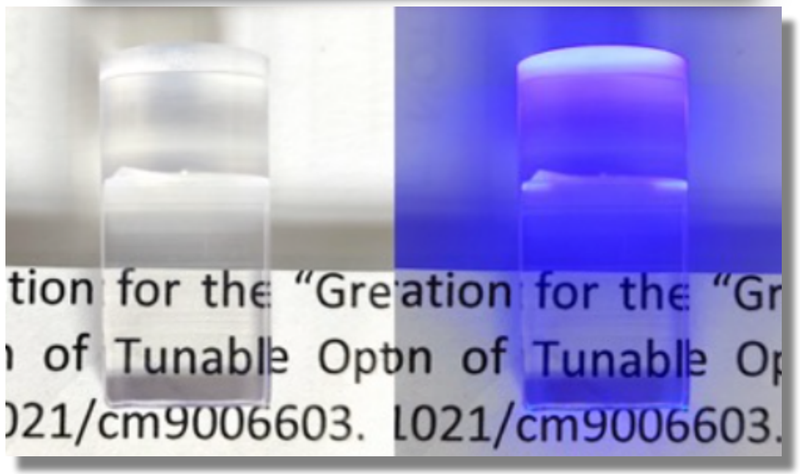
To reduce the discharge of "good" events, the probability of photoelectric absorption inside the scintillator must be maximized. Typically, inorganic scintillators are exploited due to their high atomic number.

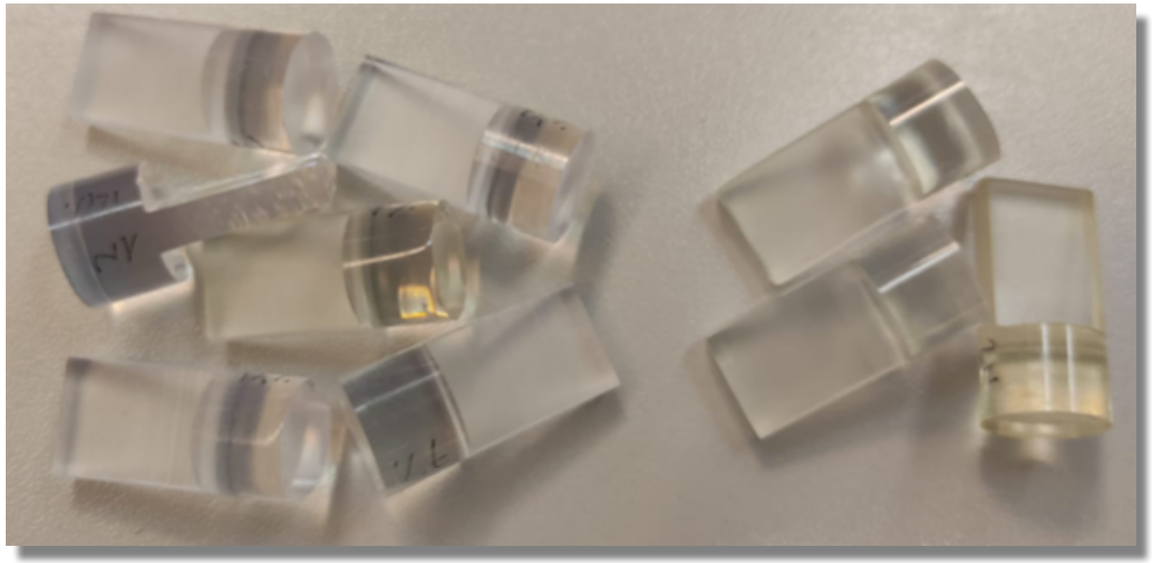


Photoelectric effect becomes dominant starting from Z≈30.

New organic scintillating molecules

- We synthesized and patented [1] several new organic scintillating molecules (T2, 2N, 1N, 2B…) containing aromatic fragments.
- We produced plastic scintillators embedding our scintillating molecules in a polyvinyl-tuoluene (PVT) matrix.
- We tested the behaviour of the fluorophores in order to choose the best candidate to make the doped samples.



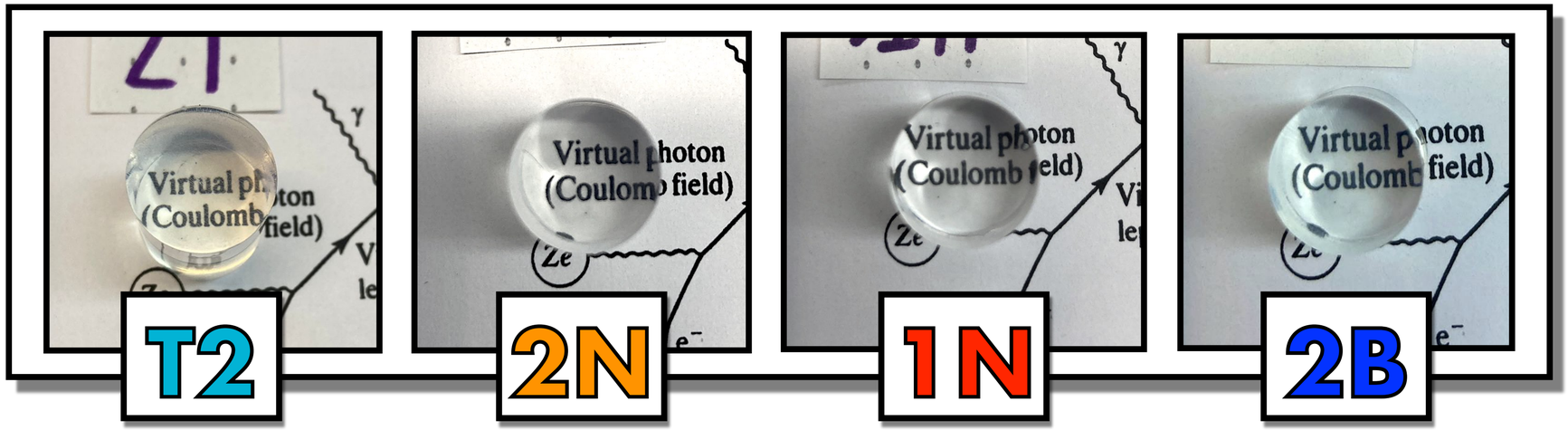


FLUOROPHORES CONCENTRATION

➡ Fluorophores concentrations ranging from 1% to 40% have been studied. The samples maintain their transparency up to 40%. Results are shown at 14%.

[1] Mattiello L.; Patera V.; Belardini A.; Rocco D.; Marafini M.; Organic Scintillator. *Patent* WO2023156957A1, 2023.

New organic scintillating molecules: performances



Light output data and timing performances have been obtained with a H10721-210 Hamamatsu PMT and a Na-22 radioactive source.

*10% systematic and statistic error

Sample	Primary dopant concentration	Light output* (wrt EJ-232)	Wavelength of max emission [nm]	Time Resolution* (@ 330 mV) [ps]	Rise Time* [ns]
EJ-232	-	100%	370 (from data-sheet)	208	2.2
BC-400	-	105%	423 (from data-sheet)	234	2.5
T2	14%	72%	420	250	2.8
2B	14%	67%	To do	224	2.4
2N	14%	103%	410	264	2.3
1N	14%	86%	To do	221	2.3

New organic scintillating molecules

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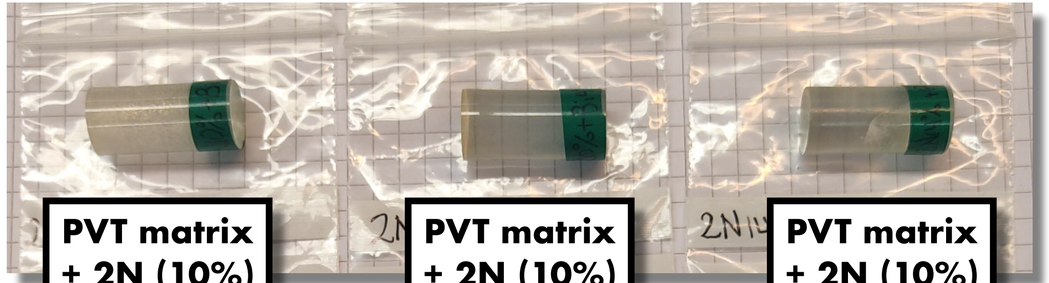
- Good light output
- No need of a wavelength shifter

Good candidate to produce the doped samples!

High-Z doped scintillator prototypes

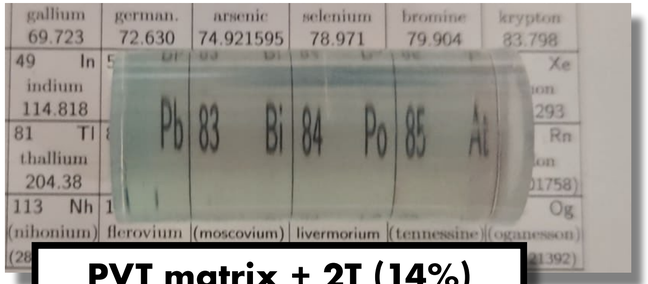
- We are producing samples of high-Z organic scintillators with different sizes, shapes and composition.
- Transparency results to be good up to very high concentrations.
- We are testing them with different radioactive sources and readout systems.



PVT matrix + 2N (10%) + Bi (2%)

PVT matrix + 2N (10%) + Bi (4%)

PVT matrix + 2N (10%) + Bi (10%)



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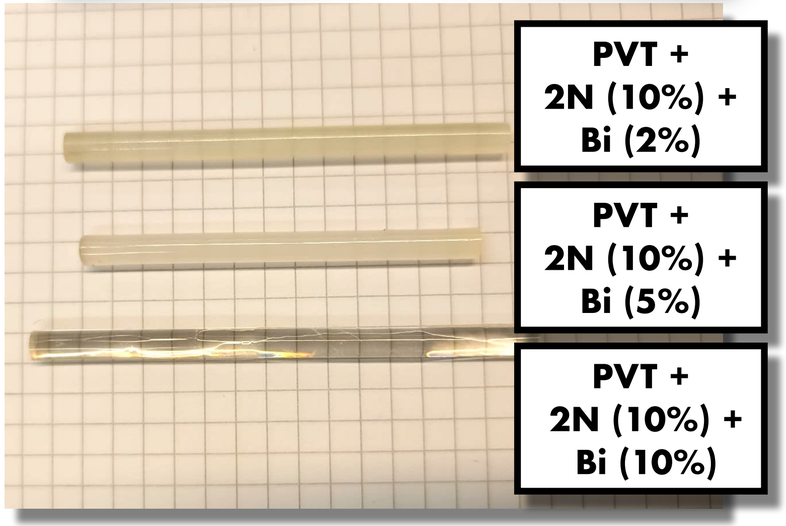

PVT + 2N (10%) + Bi (2%)

PVT + 2N (10%) + Bi (5%)

PVT + 2N (10%) + Bi (10%)

High-Z doped scintillator prototypes

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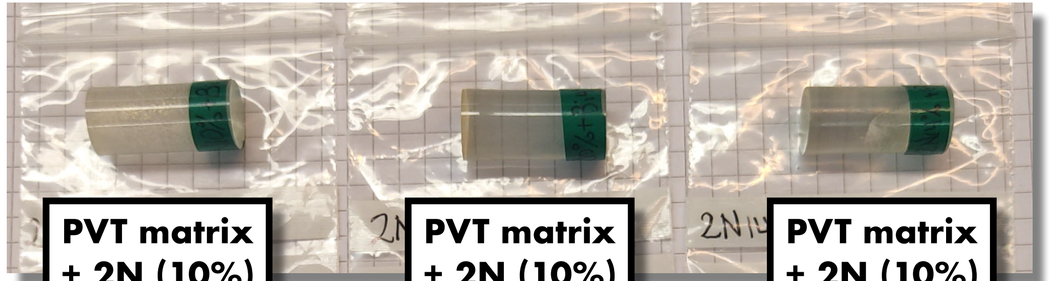

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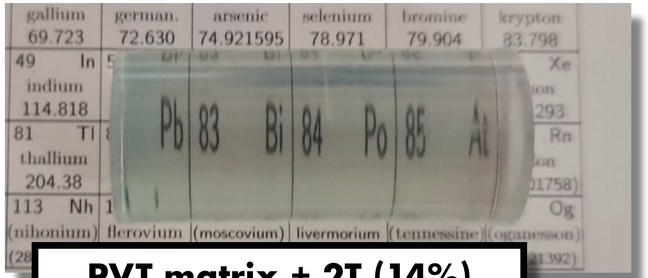
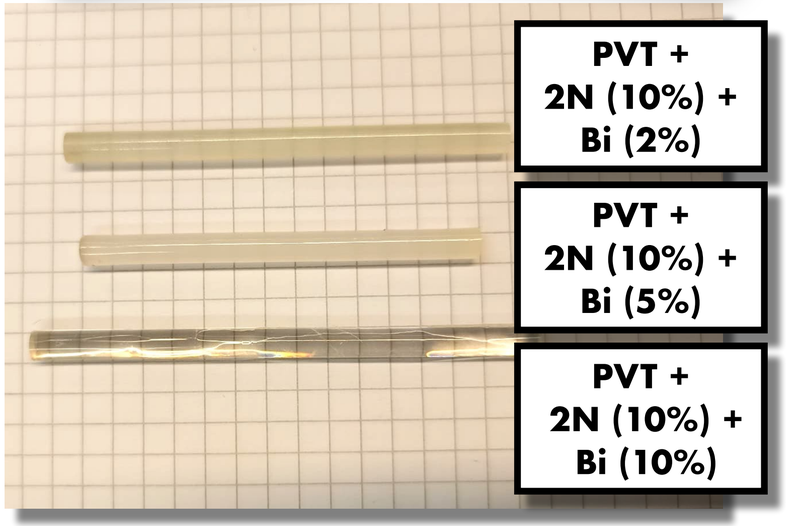


PVT matrix + 2T (14%) + Bi (4%)



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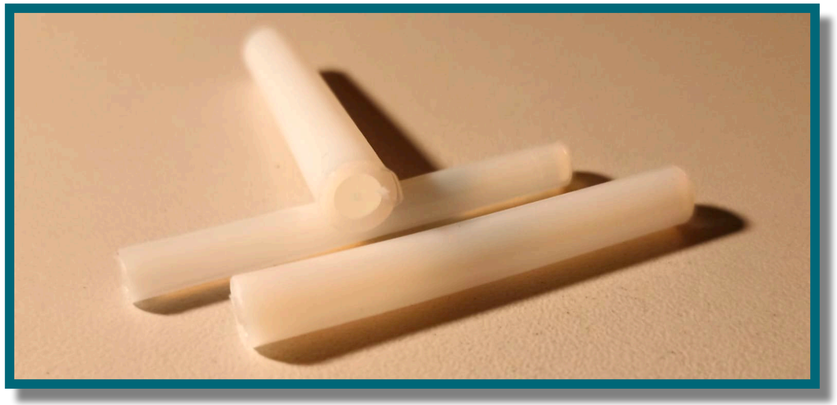


In order to improve the collection efficiency of the scintillation light, we produced samples where the polymerization process happens directly inside a PTFE (teflon) coating.

PVT + 2N(14%) + Bi(0%)

PVT + 2N(14%) + Bi(2%)

PVT + 2N(14%) + Bi(10%)

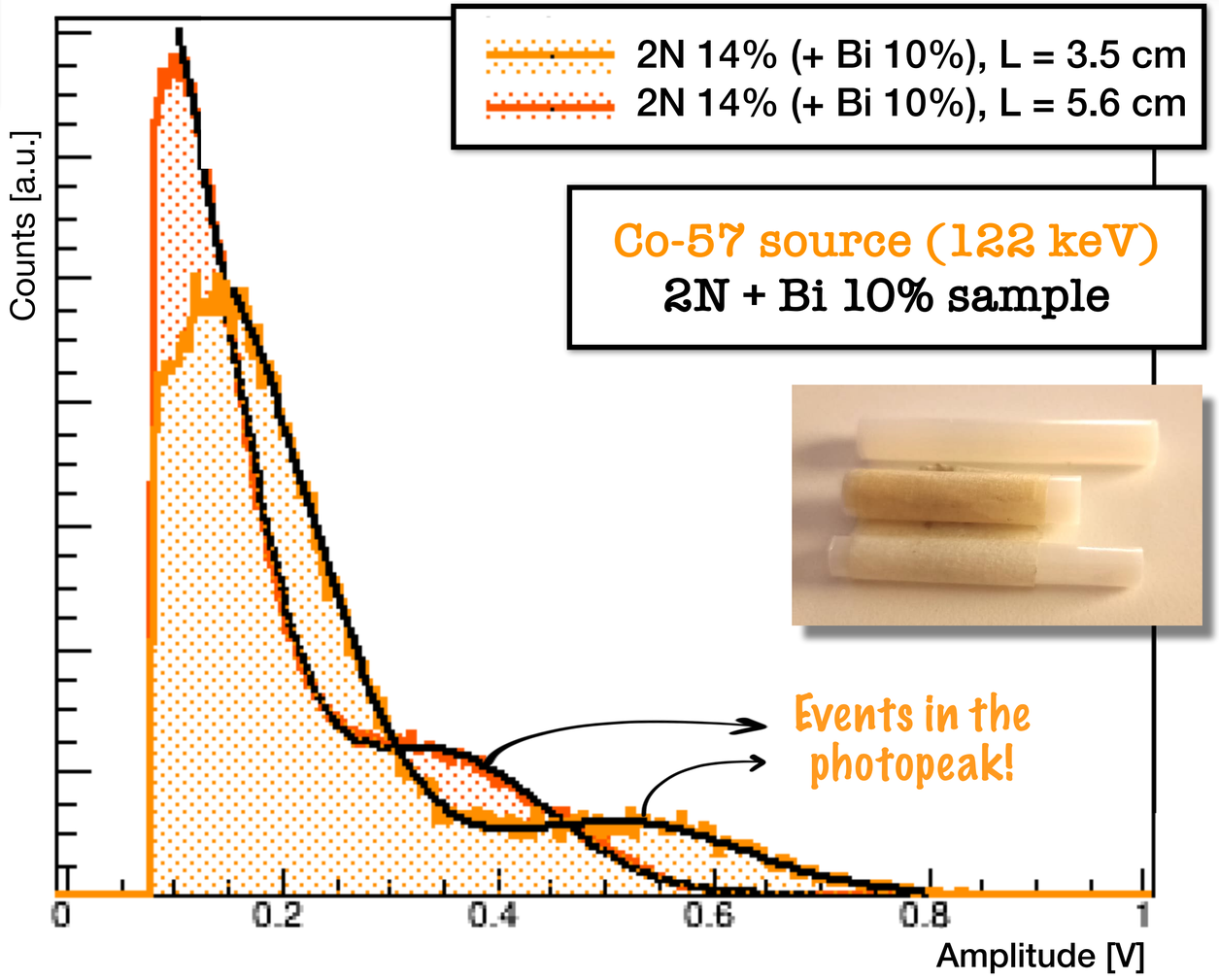
High-Z doped scintillator prototypes: performances

Ba-133 source (300 keV)
2N + Bi 10% sample

Events in the photopeak!

The addition of Bismuth does not deteriorate the time resolution!

Scintillator	Light Output [a.u.]
2N + 0% Bi	100%
2N + 2% Bi	30%
2N + 10% Bi	25%



Co-57 source (122 keV)
2N + Bi 10% sample

Events in the photopeak!

Next steps

- [x] With the reSPECT project, we are targeting a **total body SPECT**, accessible to the National Health System in terms of cost, space and diagnostic efficiency.
- [x] Characterization of our new organic scintillators is terms of light output and timing performances with promising results.
- [x] Production of a **10%-doped sample**: looking for photopeaks!
- [x] Polymerisation of the samples inside Lead, Aluminum, Teflon, PE, PTEF.

- [ ] Production of 3d-printed samples with a **resin substrate**.
- [ ] Tests with samples containing other high-Z dopants (e.g. **Erbium**) and higher concentrations.
- [ ] Data acquisitions with **Technetium-99 metastable**.
- [ ] Polymerization of the samples inside the Tungsten hive.


Prototype of Tungsten collimator

^{177}Lu-PSMA-617 treatment for mCRPC

AlphaBet: Combination of Radium-223 and [^{177}Lu]Lu-PSMA-I&T in men with metastatic castration-resistant prostate cancer (clinical trial protocol)

Louise Kostos, [1,2] James P. Buteau, [2,3,4] Theresa Yeung, [5] Juliana Di Iulio, [5] Jing Xie, [5] Anthony Cardin, [2,3,6] Kwang Y. Chin, [2,6] Brittany Emmerson, [3,4] Katie L. Owen, [2,7] Belinda S. Parker, [2,7] Heidi Fettke, [2,8] Luc Furic, [2,8] Arun A. Azad,[1,2,*,†] and Michael S. Hofman[2,3,4,*,†]

Abstract

Go to:

Background

[^{177}Lu]Lu-PSMA is a radioligand therapy used in metastatic castration-resistant prostate cancer (mCRPC). Despite a survival benefit, the responses for many patients receiving [^{177}Lu]Lu-PSMA are not durable, and all patients eventually develop progressive disease. The bone marrow is the most common site of progression. Micrometastases in this area likely receive an inadequate dose of radiation, as the emitted beta-particles from ^{177}Lu travel an average range of 0.7 mm in soft tissue, well beyond the diameter of micrometastases. Radium-223 (^{223}Ra) is a calcium-mimetic and alpha-emitting radionuclide approved for use in men with mCRPC with bone metastases. The range of emitted alpha particles in soft tissue is much shorter (≤100 μm) with high linear energy transfer, likely more lethal for osseous micrometastases. We anticipate that combining a bone-specific alpha-emitter with [^{177}Lu]Lu-PSMA will improve eradication of micrometastatic osseous disease, and thereby lead to higher and longer responses.