

Multi-dose kits for preparation of Gallium-68-PSMA-11

Introduction Nowadays, the majority of men will eventually develop prostatic diseases including prostate cancer. Due to a more personalized screening, prostate cancer may be detected relatively early. Nevertheless, current clinical care is challenged by the complexity of advanced prostate cancer and a limited number of effective treatment approaches. New strategies suggest promising biomarkers for a more precise diagnosis, whereas treatments such as peptide radioligand therapy (PRLT) offer hopes for patients with metastatic prostate cancer beyond our control. In Nuclear Medicine small molecules targeting prostate-specific membrane antigen (PSMA) have emerged as highly potent imaging agents, however; efficient radiolabeling procedures combined with a steadily growing need for safe and fast radiopharmaceutical production can create strategic problem. We addressed this by developing a kit-based radiolabeling solution providing [⁶⁸Ga]Ga-HBED-CC-(Ahx)-Glu-Urea-Lys ([⁶⁸Ga]Ga-PSMA-11, Fig.1) in a fast, "shake-and-bake"-like tracer production (1).

Methods Batch PSMA-11 kit manufacturing was followed by radiolabeling with ⁶⁸Ga-activity from a 50 mCi ⁶⁸Ge/⁶⁸Ga-generator. Kits were heated for 5 min at >90°C and were analyzed for instant radiolabeling (no further purification required) (Fig.2). [⁶⁸Ga]PSMA-11 product quality was tested for radiochemical purity and yield, radionuclidic purity, pH and sterility. Patient administration was done within 150 min of radiopharmaceutical production. The kit performance to warrant instant [⁶⁸Ga]PSMA-11 radiolabeling was further challenged by changing the kit shelf-life, storage, quality and acidity of the ⁶⁸Ga-activity and the generator type.

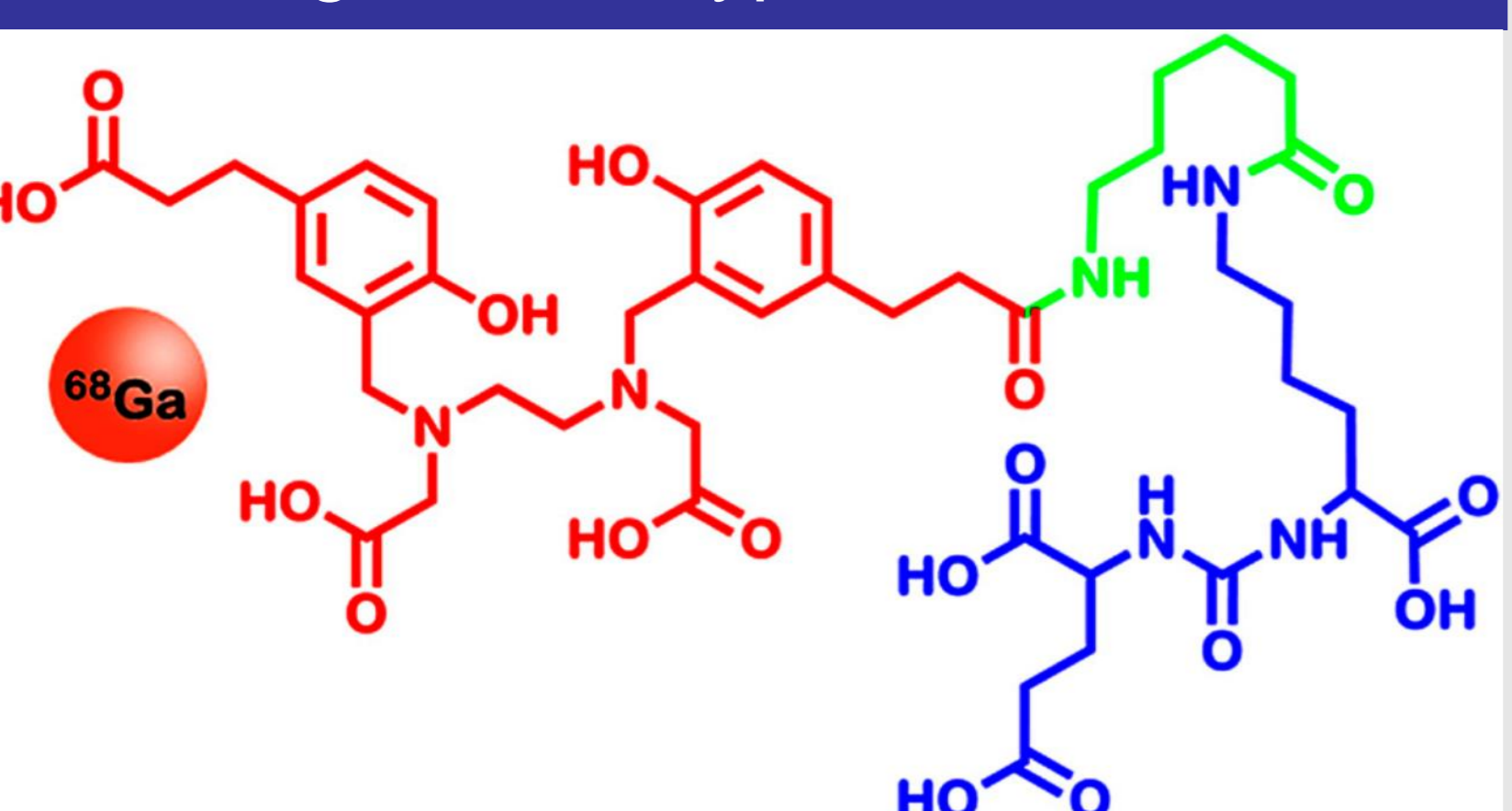


Fig 1. Structure of [⁶⁸Ga]Ga-HBED-CC-(Ahx)-Lys-Urea-Glu

References

1.Ebenhan, T. et al., Molecules. 2015;20(8):14860-78

[⁶⁸Ga]Ga-PSMA-11 production

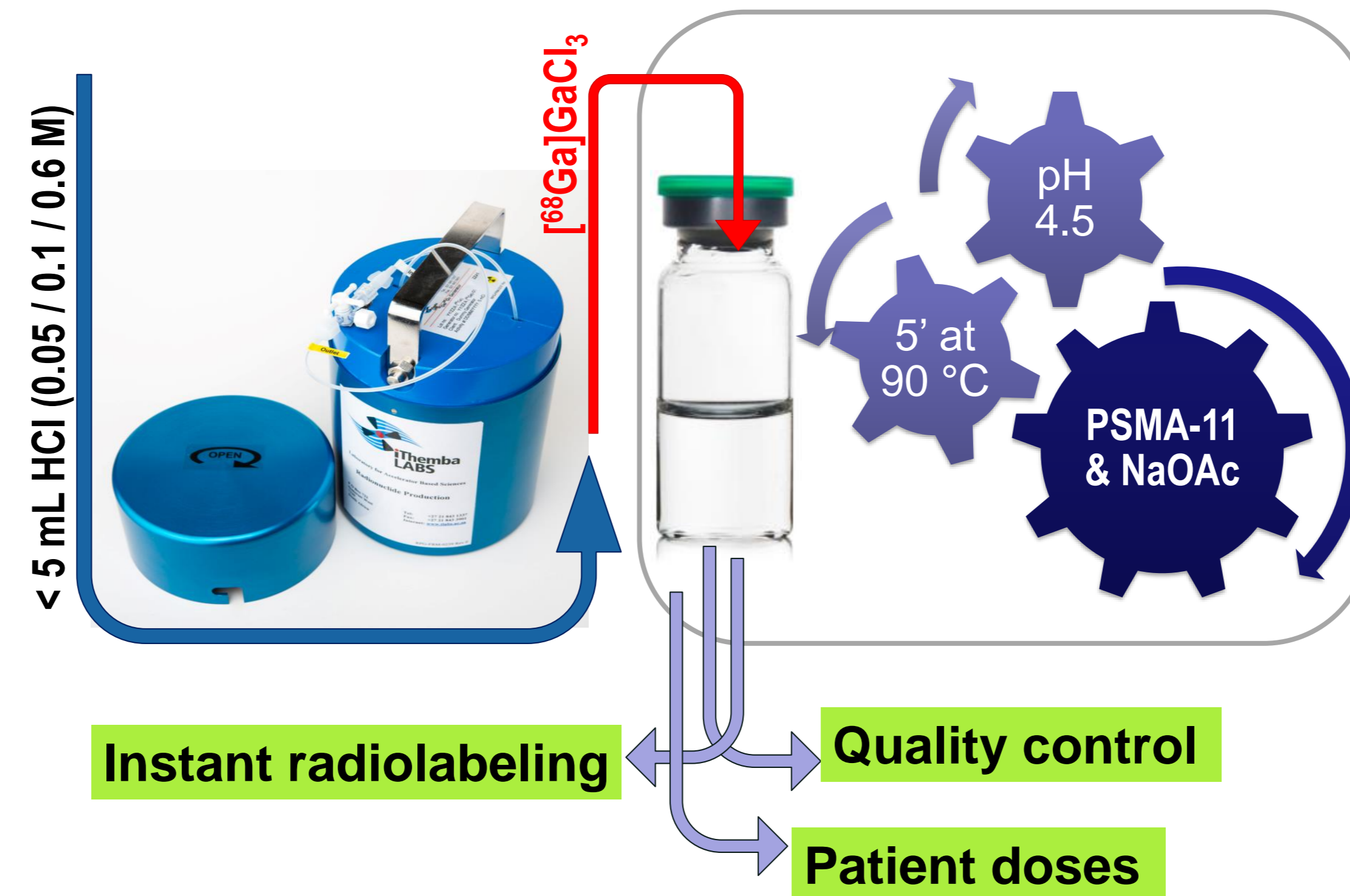


Fig 2. Generator elution (blue arrow) provides ⁶⁸Ga-activity by simple volume fractionation, which can be used immediately for kit radiolabeling (red arrow). The ⁶⁸Ga-activity reacts with the kit contents designed to provide instant radiolabeling. This PSMA-11 kit is universally applicable to ⁶⁸Ga-activity from different generators*.

*) Generators types used: 1) ITG Garching, 2) iThemaLABS; 3) Eckert & Ziegler

Tab 1. Summary of [⁶⁸Ga]Ga-PSMA-11 kit radiosyntheses

Parameter	Criteria	Kit Specification
Radiosynthesis (N)		circa 500
Added activity		678 ± 240 MBq
Labeling efficiency (LE)	> 50 %	91 ± 8 %
Production time	< 45 min	21 ± 3 min
PSMA-11 mass/ kit	5.0 ± 1.0 µg	4.8 ± 0.5 µg
Instant Radiolabeling		381/458 (83 %)
Activity losses (vial)	- 10 %	- 5.1 ± 1.2 % (N=177)
*C18 SPE losses (N)	- 15 %	- 8.5 ± 5.4 % (N=177)
Molar activity	> 20 GBq/µmol	186 ± 39 GBq/µmol
Radiochemical purity	> 95 %	98.8 ± 0.7 %
Euate volume E&Z	1.10 – 4.00 mL	> 95 % (N = 8)
Euate volume ITG	1.50 – 5.00 mL	> 95 % (N = 6)
Euate volume iTL	0.74 – 1.25 mL	> 95 % (N =30)
pH for injection	neutral	passed

Generators types used: ITG) ITG Garching, iTL) iThemaLABS; E&Z) Eckert & Ziegler

[⁶⁸Ga]Ga-PSMA-11 kit performance

- ✓ **One production** [⁶⁸Ga]PSMA-11 = **4 patients**
- ✓ **2 doses** can be warranted over the **9 months** generator life-span.
- ✓ The kit radiolabeling solution was **universally applicable** to **3 different generator** types.

Tab 2. Patients population data and parameters for safe [⁶⁸Ga]Ga-PSMA-11 administration

Parameter	Specification	[⁶⁸ Ga]Ga-PSMA-11 injection
Radiosynthesis yield	> 200 MBq	455 ± 87 MBq
Radiation exposure / synth.		16.6 ± 5.8 µSv
Sterility		passed
Endotoxins	<10 EU	passed
% Germanium	< 0.001	passed

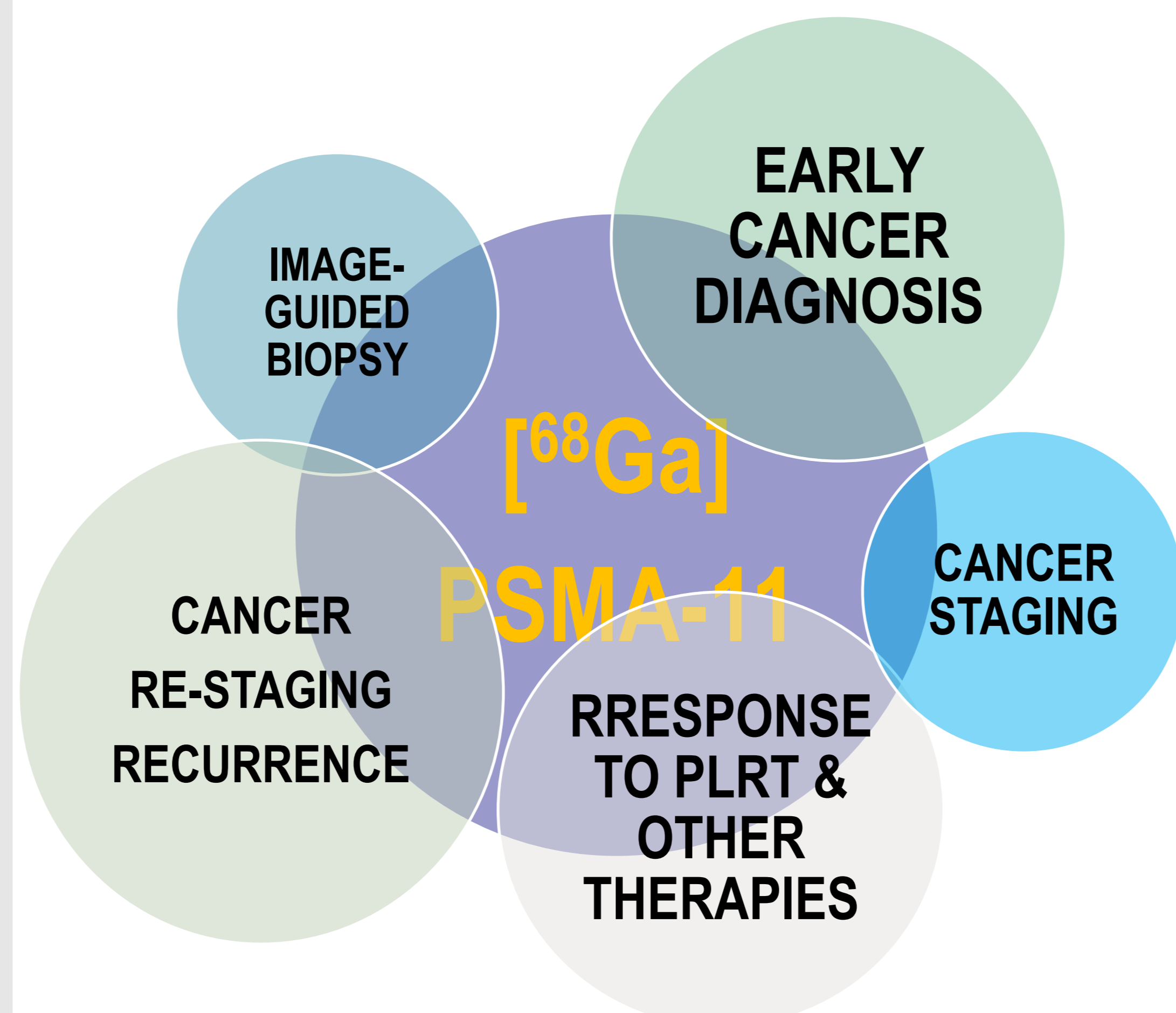


Fig 3. The kit sensitivity supporting the displayed imaging scenarios.

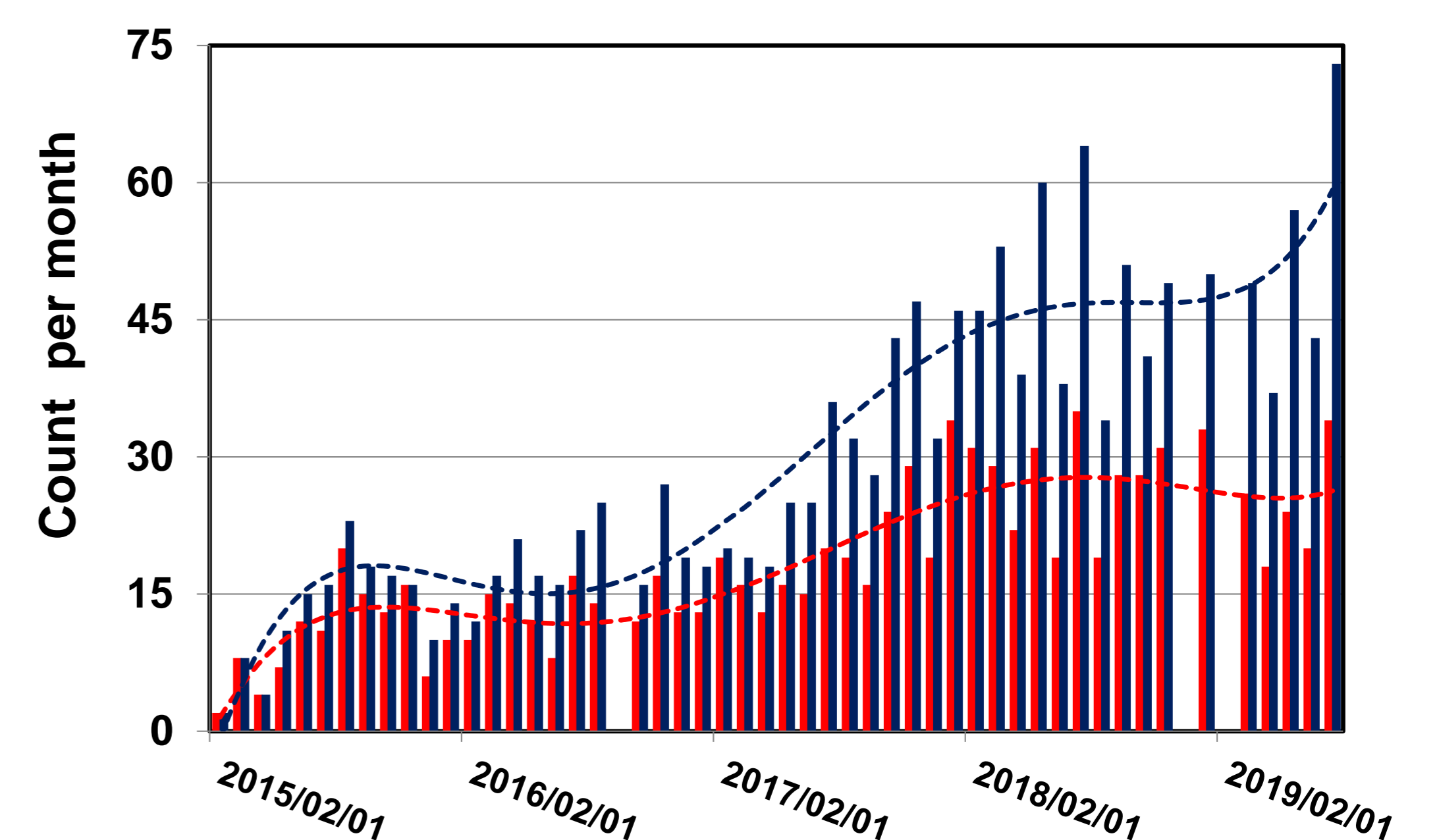


Fig 4. Monthly production chart: red: number of radiosyntheses; dark-blue: number of patients injected

Kit based preparation of [⁶⁸Ga]Ga-PSMA-11 has a well documented impact and tremendous value in supporting better PET/CT imaging and therapy of prostate cancer.

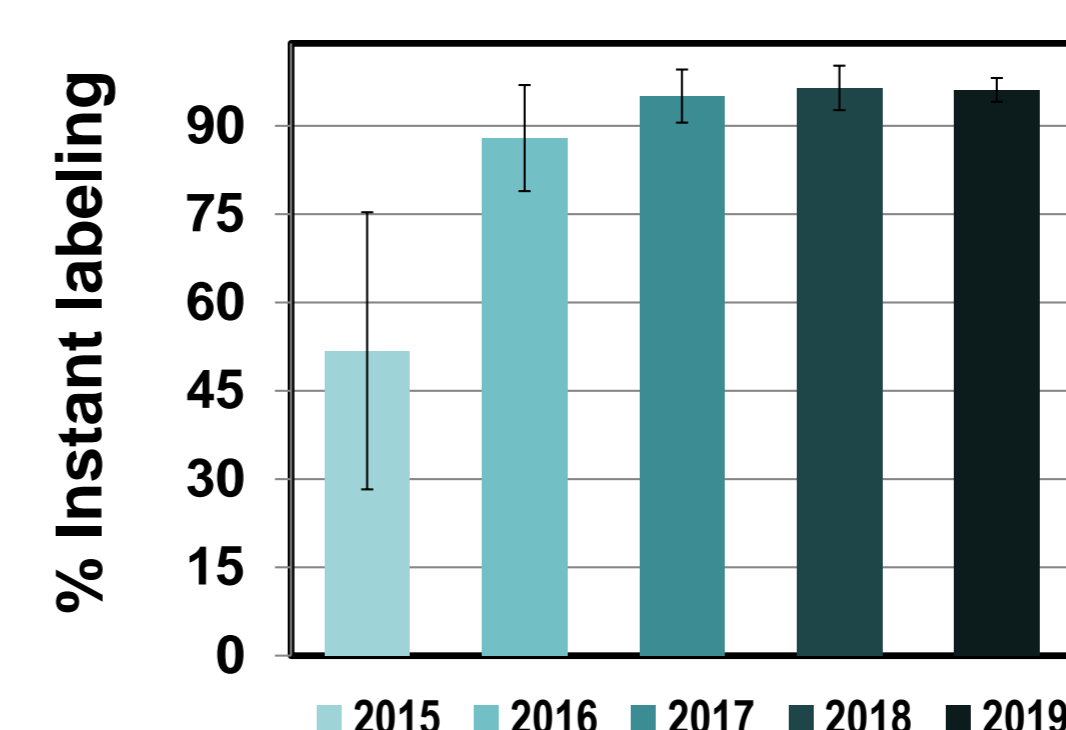


Fig 5. PSMA-11 kit radiolabeling performance: Number of kits labeled / yr : 2015 = 114; 2016 = 147; 2017= 206; 2018 = 284; 2019* = 295

* projections based on (Jan-Jun)