Routine Production of [^{18}F]PSMA-1007 and First Clinical Experience in Staging of Prostate Cancer Patients

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Introduction

- Prostate-specific membrane antigen (PSMA) is highly overexpressed in prostate cancer (PCa) and considered an ideal target for staging of primary and recurrent PCa [1]
- Different PSMA-targeting PET radiopharmaceuticals have been introduced which showed to be superior in comparison to standard of care (see Fig. 1)

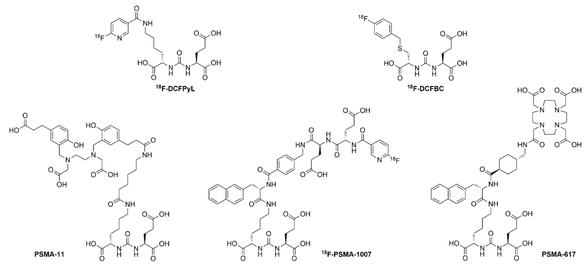

Figure 1: Different PSMA-Ligands in clinical practice

- Despite their excellent imaging properties, ^{68}Ga-labelled PSMA-tracers can only be produced in small amounts and distributed over short distances, limiting their availability for broader application
- Recently, [^{18}F]PSMA-1007 has been introduced, combining the possibility of centralized, large-scale production and higher spatial resolution for PET imaging [2]. Clinical results indicate further advantages such as higher tumor-to-background ratios and low renal excretion [3]

Objective

- Cardinale et al. described the GMP-compliant production and quality control of [^{18}F]PSMA-1007 in different synthesis modules and using starting activities of up to 75 GBq [4]
- Our objective was to evaluate the influence of higher starting activities on radiochemical yields (RCY), radiochemical purity (RCP) and stability of the final product
- We furthermore wanted to confirm the clinical results reported for PSMA-1007 in terms of sensitivity and specificity for the staging of primary PCa

Materials & Methods

- [^{18}F]PSMA-1007 was produced under GMP-compliant conditions on the IBA Synthera® platform using commercially available Kits and the same procedure as described previously (see Fig. 2)

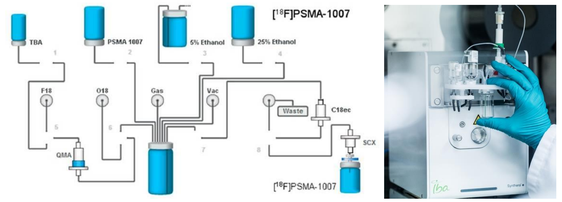

Figure 2: Fluidic scheme PSMA-1007 cassette

- Briefly: 1) ^{18}F-Fluoride trapped on QMA, 2) elution with 75 mM TBA, 3) adding 1 mg precursor in 1.5 mL DMSO, 4) heating 10 min at 95° C, 5) purification via C18ec cartridge, cleaning with 5% EtOH, fractionated elution with 25% EtOH via SCX and reformulation in ascorbic acid buffer
- RCP was determined via Radio-HPLC: column: Poroshell, Agilent, C18ec 50x4.6-mm, solvent A: acetonitrile, solvent B: 0.1% TFA, Flow: 1.5 mL/min, gradient: Solvent A 5-15% in 1 min, 15-35% in 9 min, 35-95% in 2.5 min and 95-5% in 2.5 min
- Stability was determined via radio-HPLC after final product has been stored at RT under exclusion of light for 8h
- Five patients (68±6 years; PSA = 14.8±4.8; GS = 7-9) with biopsy confirmed PCa underwent a diagnostic PET/CT (Biograph mCT20, Siemens) 66±9 min. after injection of 7.5±0.4 mCi [^{18}F]PSMA-1007. All patients had local disease and underwent radical prostatectomy and lymph node dissection 54±16 days after PET. Immunohistochemistry (IHC) results were compared with PET findings to determine sensitivity, specificity, PPV, NPV and accuracy

Case	Age	PSA	Gleason	PET - LN	Histology
1	74	12.8	4+4	0	Prostate(+), LN(-) 0/39
2	60	13.6	9	9	Prostate(+), LN(+) 7/16
3	74	8.7	8	0	Prostate(+), LN(-) 0/19
4	67	21.0	4+3	3	Prostate(+), LN(+) 3/20
5	65	18.0	4+3	0	Prostate(+), LN(+) 1/10

Results

- The production procedure described for the IBA Synthera platform is very reliable and provides excellent RCYs in 35 minutes after EOB
- RCYs were determined as non decay corrected yields at EOS. From starting activities of 78.2±31.8 GBq we obtained an average of 41.4±16.5 GBq [^{18}F]PSMA-1007 corresponding to 53.9±8.2 % RCY n.d.c., n = 21) with 95.2±2.4 % RCP (see Tab. 1)

Table 1: Starting activities, RCYs, RCPs and specific activities

N°	[18F]F GBq	Product GBq	RCY / %	RCP / %	Sa / GBq/µmol
n=7	42.8±9.1	26.8±7.1	62.5±10.1	95.8±1.0	628±285
n=20	73.1±10.0	38.5±6.2	52.9±6.7	94.9±2.5	1017±575
n = 8	117.8±38.7	59.5±23.1	49.9±6.0	95.4±2.8	1980±970
n=1	212.6	114.1	53.7	91.2	3344

- Higher starting activities resulted in lower but still very good RCYs and specific activities while RCPs maintained stable slightly above 95%
- We found the labeling process and RCYs to be much more affected by non-radioactive impurities from target, fittings or transfer lines as compared to other processes, e.g. FDG
- No radiolysis was observed in final product and RCP was stable up to 8h after EOS
- [^{18}F]PSMA-1007 showed excellent image quality, low renal excretion and higher SUV values as compared to [^{68}Ga]PSMA

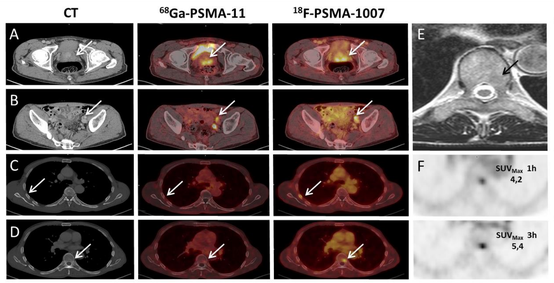

Figure 3: PET/CT scans with ^{68}Ga-PSMA-11 and ^{18}F-PSMA-1007 of case 4

- Preliminary results confirm the very good sensitivity and specificity although the size of the study group is very small. Further studies are ongoing to increase population size and significance of our results.

		Histology		
		+	-	∑
PET	+	10	2	12
	-	1	103	104
	∑	11	105	

Sensitivity:	90.9 %
Specificity:	98.1 %
PPV:	83.3 %
NPV:	99.0 %
Accuracy:	97.4 %

Figure 4: Sensitivity and specificity for LN detection in pPCa

Conclusion

- [^{18}F]PSMA-1007 can be obtained in excellent and reliable radiochemical yields and purities by the process described.
- Our first results confirm the excellent imaging properties and underline the clinical potential of this new tracer
- Further studies are necessary to confirm PET positive lesions in lymph nodes and metastasis by histopathology

References

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4. Cardinale et al., GMP-compliant production of 18F-F-PSMA-1007, Pharmaceuticals, 2017, 10 77

Disclosures

Disclosure: René Martin, Anna-Maria Zerges and Marco Müller are employees of ABX advanced biochemical compounds GmbH. The one-step synthesis method using Precursor 3 is the subject of a patent application by ABX advanced biochemical compounds. Cristiana Gameiro and David Goblet are employees of IBA.

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