THERANOSTICS EARL

GUIDANCE

EARL THERANOSTICS

VERSION 1.1

September 2025

This guidance provides the background of the EARL Theranostics certification for centres to become a EARL Qualified Theranostics Centre of Excellence (level 1 and 2), with a short description of the context and detailed instructions for submitting the required information.

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REVISIONS

Date	Version	Description of changes
01Jul2024	1.0	Initial release
29Sept2025	1.1	Level 2 release

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INTRODUCTION

The EANM has established a Theranostics Centre of Excellence (CoE) network to promote a harmonised, high-quality approach to theranostics across accredited institutions. These specialised centres, dedicated to delivering advanced, personalised theranostics procedures, serve the best interests of patients while also supporting other key stakeholders, including industry partners and regulatory bodies.

Delivering optimal patient care is central to advancing personalised medicine. However, medical innovations must be rigorously validated by qualified experts within certified centres, in accordance with defined quality standards. A CoE must therefore offer a robust clinical service, encompassing a broad range of treatment options, cutting-edge technologies, and consistently high standards of care. Enroll now and be on the map as a Centre of Excellence for Theranostics. To view the currently enrolled EARL Theranostics Centres of Excellence in level 1 and 2, please zoom in on the map and click the pin for more details.

The theranostics concept – using the same target for both imaging and therapy – has been a core principle of nuclear medicine since the 1940s, starting with iodine-131 (^{131}I) in thyroid disease. Although early agents like ^{131}I and yttrium-90 (^{90}Y) radiolabeled anti-CD20 antibodies achieved strong outcomes in low-grade Non-Hodgkin Lymphomas[1,2,3], they were largely replaced by non-radioactive therapies, mainly due to market dynamics and easier administrations. The success of iodine-based theranostics and the approval of [^{177}Lu]Lu-DOTATATE for gastroenteropancreatic neuroendocrine tumours (GEP-NETs), based on the NETTER-11 trial, have broadened the use of targeted radionuclide therapies (tRNT). Applications now extend to higher-incidence diseases like prostate cancer. The TheraP and VISION trials[4,5] demonstrated that [^{177}Lu]Lu-PSMA-617 significantly improves overall survival[2] in metastatic castration-resistant prostate cancer (mCRPC), resulting in the approval of [^{177}Lu]Lu-PSMA-617 by FDA and EMA.

While ^{177}Lu-based tRNT is effective, response rates and long-term outcomes can still be improved. Over the last years, a new generation of α-emitting tRNT agents has emerged. Several studies[6,7,8,9,10,11,12] have demonstrated the efficacy of Targeted Alpha Therapy (TAT), particularly with [^{225}Ac]Ac-DOTATATE and [^{225}Ac]Ac-DOTATOC[13,14] in β-refractory NET patients. Given that 18–32% of patients are resistant to β-emitting [^{177}Lu]Lu-DOTATATE therapy[15], TAT may serve as an adjuvant therapy. Similarly, in mCRPC [^{225}Ac]Ac-PSMA has shown high efficacy in heavily pre-treated patients resistant to multiple prior therapies, including [^{177}Lu]Lu-PSMA[16,17,18,19,20,21,22,23].

This growing evidence base has led to a surge in demand for theranostics procedures, presenting both challenges and opportunities for healthcare systems. Even in countries with a strong tradition in radionuclide theranostics, existing infrastructure may be insufficient[24,25]. Therefore, preparing for this demand from patients, physicians, and society, is essential.

This guide supports stakeholders interested in registering their centre within EARL's Theranostics Centre of Excellence network.

The EARL Theranostics certification programme includes three levels: Qualified, Advanced and Educational Centre. Following the launch of Level 1 (Qualified), the Level 2 Advanced Theranostics Centre of Excellence is now available.

THERANOSTIC CERTIFICATION LEVEL 2

This manual covers Level 2, focusing on centres with an established theranostic structure and aims to assess their capacity to deliver high-quality, integrated, and advanced theranostic services. Special attention is given to existing infrastructure, technical implementation, clinical integration, staffing levels and training, as well as compliance with applicable regulatory frameworks.

As this certification programme is complementary to the existing EARL PET and SPECT certification programmes, participating centres are expected to already hold these relevant accreditations. Specifically, centres must hold a valid EARL PET/CT [^{18}F] Standard 1 or 2 accreditation at the time of application. Centres must document sufficient procedure volumes, effective collaboration among nuclear medicine physicians, radiopharmacists, medical physicists, and technologists, and have structured staffing and training policies in place. Production of radiopharmaceuticals, when applicable, must comply with national regulations and good manufacturing practices.

To qualify as a Level 2 Advanced Theranostics Centre of Excellence, applicants must also meet a set of more stringent clinical and structural requirements. The centre must include at least one board-certified nuclear medicine physician, or equivalent, according to national legislation. All staff involved in theranostic activities must be up to date with continuing education, in compliance with national regulations. In terms of infrastructure, direct access to PET/CT or PET/MRI systems on-site is not mandatory, provided a formal collaboration is established with another institution that offers these imaging modalities. However, access to a SPECT/CT system is essential, and systems limited to organ-dedicated imaging do not fulfil this requirement. Furthermore, a minimum volume of 250 administrations per year across all theranostic therapies is required.
At least one radionuclide calibrator must be available on site, although traceability to a national standard is not mandatory. The clinical practice of the centre must reflect sufficient diversity and experience. Applicants must document the routine treatment of at least two different malignancies, using two different radiopharmaceuticals and two different radionuclides.

This certification step will identify centres prepared to meet more advanced expectations in clinical theranostics and will serve as a foundation for further qualification, including possible participation in future educational and research initiatives under Level 3 certification.

The next section provides an overview of the theranostic procedures considered within the scope of Level 2 certification. It is followed by a summary of relevant EU regulatory aspects and an outline of the quality and safety domains assessed during the certification process, beginning with patient stratification.

THERANOSTIC PROCEDURES

Below are listed the most established, new, and emerging theranostic procedures which can be covered by an EARL Qualified Theranostics Centre of excellence.

Thyroid disease

[^{131}I]-based treatment for managing and treating benign thyroid disease and thyroid cancer[26,27]

- Therapeutic radiopharmaceutical: [^{131}I]NaI
- Diagnostic procedure: [^{99m}Tc]Tc- or [^{123}I]I-scintigraphy or [^{124}I]I-PET

Neuroendocrine tumours

- [^{131}I]-based treatment for managing unresectable, locally advanced or metastatic[28] pheochromocytoma, paraganglioma or neuroblastoma requiring systemic anticancer therapy, with the suitability for treatment confirmed
  - Therapeutic radiopharmaceutical: [^{131}I]mIBG
  - Diagnostic procedure: [^{131}I]I-SPECT/CT

- Peptide Receptor Radionuclide Therapy (PRRT)[29] targeting the somatostatin type 2 receptor (SSTR2), which is overexpressed on the membrane of neuroendocrine tumour (NET) cells
  - Therapeutic radiopharmaceutical: [^{177}Lu]Lu-DOTATATE (Lutathera, Novartis), which has been approved by the European Medicines Agency (EMA, 2017) and American Food and Drug Administration (FDA, 2018) as PRRT for patients with gastroenteropancreatic neuroendocrine tumours (GEP-NETs) overexpressing SSTR2 who have metastatic disease and therefore are not eligible for surgery or other SSTR targeting ligands for the same indication (e.g. [^{177}Lu]Lu-DOTATOC, [^{177}Lu]Lu-DOTANOC). Additionally, other SSTR2 agonists and antagonists being employed for PRRT, labeled with other beta emitters like ^{161}Tb or ^{90}Y or with alpha emitters like ^{225}Ac.
  - Diagnostic procedure: PET imaging with the corresponding ^{68}Ga or ^{18}F labeled SSTR2 (ant)agonist

Prostate cancer

PSMA (prostate-specific membrane antigen) radioligand therapy (PRLT)[30] targeting PSMA that is overexpressed on the membrane of prostate cancer cells.

- Therapeutic radiopharmaceutical: [^{177}Lu]Lu-PSMA-617 (Pluvicto, Novartis), which has been approved by the FDA (2022) and EMA (2022) as PRLT for patients with progressive, PSMA-positive metastatic castration-resistant prostate cancer (mCRPC) or other PSMA-targeting radioligands (e.g. PSMA-I&T) for the same indications. Additionally, PSMA labeled with other beta emitters like ^{161}Tb or alpha emitters like ^{225}Ac is employed for PRLT
- Diagnostic procedure: PET imaging with the corresponding ^{68}Ga- or ^{18}F-labeled PSMA ligands.

Liver disease

Radioembolization treatment with intra-arterial radioactive compounds of liver cancer and liver metastases, including hepatocellular carcinoma and liver metastatic colorectal cancer.

- Therapeutic radiopharmaceutical: Resin or glass microspheres labelled with ^{90}Y or alternatively ^{166}Ho-microspheres.
- Diagnostic procedure: pre-treatment intra-arterial ^{99m}Tc-labelled albumin macroaggregated albumin1 (^{99m}Tc-MAA) scintigraphy to quantify potential liver-lung shunting and exclude reflux to bowel, stomach or pancreas. For ^{166}Ho-microspheres radioembolization, administration of a scout dose of ^{166}Ho-microspheres can be considered as it is safe and more accurate for the calculation of the lung shunt fraction when compared to ^{99m}Tc-MAA

Bone metastases

- Alpha therapy of bone metastases in patients with metastatic castration-resistant prostate cancer and no known visceral metastatic disease
  - Therapeutic radiopharmaceutical: [^{223}Ra]Radiumdichloride
  - Diagnostic procedure: 99mTc-labeled radiopharmaceuticals for bone scan, or [^{18}F]-Fluoride-PET/CT with evidence of bone metastases and cross-sectional imaging of thorax and abdomen, e.g. with CT/MR or hybrid PET/CT or PET/MR (possible tracers: [18F]-Fluorethylcholine, [11C]-Choline, and [68Ga]-PSMA)
- Beta therapy of bone metastases in cancer patients

- Therapeutic radiopharmaceutical: bone-seeking beta-emitting radiopharmaceuticals such as strontium-89 (^{89}Sr) or samarium-153 (^{153}Sm) lexidronam (^{153}Sm-EDTMP), both approved in EU and US and phosphorus-32 (^{32}P) sodium phosphate, only approved in US.
- Diagnostic procedure: bone scan or [^{18}F]-Fluoride-PET/CT

EU REGULATIONS

Institutions applying for the EARL Theranostics registration must comply with all relevant local regulations. Where national rules are absent, adherence to the International Basic Safety Standards (BSS)[31] by the International Atomic Energy Agency (IAEA)[32] is recommended. The European Commission Directive 2013/59/EURATOM[33] for EU countries, transposed into national law by the Member States, incorporates BSS and ICRP recommendations and sets binding requirements for all exposure situations relevant to theranostic centres.

Chapter VII on medical exposure highlights the need to balance diagnostic or therapeutic benefits against the individual detriment, while considering alternative techniques with lower or no radiation exposure (Article 55). Therapeutic exposures shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose, while doses to non-target volumes and tissues shall be minimised (Article 56). Also, the different levels of involvement by a medical physics expert (MPE) are described (Article 58), with close involvement necessary for non-standardised radiotherapeutic nuclear medicine practices.
Operating a theranostic centre requires a radioactive material license (RAM) granted by national authorities, covering both diagnostic and therapeutic radiopharmaceutical use, as defined in ICRP Publication 105[34]. Obtaining this license requires adequate infrastructure, trained personnel (physicians, technologists, nurses, radiation safety officer, MPE), radiation protection measures, and procedures for managing discharged patients and radioactive waste, tailored to the diagnostics and therapies applied.

ADMINISTRATION OF RADIOPHARMACEUTICALS

Accurate quantification of the administered radioactivity is essential and relies on radionuclide calibrators traceable to primary standards[35,36,37].
A robust quality assurance (QA) and quality control (QC) programme ensures reliable, safe and reproducible equipment operation and proper clinical administration of radiopharmaceuticals[9,38,39]. Acceptance testing after installation must confirm compliance with performance specifications and establish a QC baseline. QC types and frequency should follow national guidelines.

Theranostic compounds must be administered with adequate shielding to avoid undesirable beta and gamma irradiation and to minimise the risk of contamination, e.g. by using hybrid shielding consisting of layers of polymethyl metacrylate (PMMA) and lead/tungsten. A syringe is prepared with the therapeutic agent, and the qualified operator administers the drug via correctly placed and patent intravenous access. This is followed by flushing with saline. For agents such as PSMA ligands, bolus administration is not required. Alternatively, semi- or fully automated infusion pumps are recommended to reduce staff radiation exposure.

RADIATION PROTECTION

Effective radiation protection requires appropriate shielding of syringes, vials, waste and storage containers to reduce external exposure to staff, the public and patients. After administration of the radiopharmaceutical, patient isolation may be necessary depending on local regulations and the radiopharmaceutical used. Shielding needs vary by type of radiation and may include PMMA boxes, lead/tungsten shielding, or concrete bunkers. All infrastructure must comply with national regulations and be in place before use.

A formal radiation risk assessment must be documented, using methods such as Failure Mode and Effects Analysis (FMEA) or Fault Tree Analysis (FTA), to demonstrate the adequacy of protective measures. U.S. centres must also comply with NRC and state-specific regulations.

Among the most widely used theranostic radionuclides is 177-lutetium [^{177}Lu], which emits beta particles with half-life of 6.7 days. Depending on the production route, small quantities of metastable lutetium-177 (^{177m}Lu) with a half-life of 161 days may be present in the final compound. In this case, ^{177m}Lu may account for approximately 0.02% of the total amount of ^{177}Lu in the final radiopharmaceutical. This requires special consideration in terms of storage and disposal of waste depending on local regulations.

Storage of Radiopharmaceuticals

Radiopharmaceuticals must be stored securely controlled environments (such as refrigerated or frozen), with access limited to authorised personnel. Storage facilities must ensure protection against theft, fire, and chemicals hazards. Transport and movement of radioactive materials to, from, and within the hospital must be carefully documented so that any radioactive material can be tracked from source to final use and disposal.

Radioactive Waste

Radioactive waste containing short-lived radioisotopes (half-life of less than 100 days) must be stored for decay prior disposal. “Clearance is the removal of radioactive material from regulatory control provided that the radionuclide concentrations are below specific clearance levels”[40].

EARL feedback

Information about the theranostics certification acceptance or rejection is provided via email. If the certification is granted, your site’s name, address and department head and primary contacts will be listed on EARL’s website in the Theranostics Centres of Excellence network. You will receive via email a certificate and signet. The certificate contains your institution name, the department, therapies provided for the respective year.

The certification signet will be provided via email as soon as the certification has been granted. You are allowed to use the certification signet (see an example below) on your correspondence and website.

If the certification is not granted for the respective level, our team will discuss with you the reasons and provide detailed feedback on the necessary steps to achieve the certification.

Enrollment submission timelines

There are no specific timelines for certification enrollment. However, the renewal period is 01-31 March. Initial feedback on the enrollment status is provided within one month of the full data submission, and a notification that the application process has started.

Yearly renewal is required. The above timelines are applicable to renew your institution's EARL Theranostics certification. Delinquency to submit the renewal form will result in suspension of the certification.

CERTIFICATION ON HOLD

Please submit enrollment/renewal form on time as noted above in the timelines section. If the deadlines are disregarded, your certification is no longer active. Re-entry into the certification programme is possible as soon as you are able to fulfil these requirements again.

CERTIFICATION FEE

The fee for the theranostics certification programme is per calendar year per site (regardless of when the process starts within the calendar year), covering the costs for the initial certification procedure and maintaining the status of an EARL Theranostics Centre of Excellence. For Level 1 there is no fee. A fee of € 1,000.00 net applies for Level 2 certification. For up-to-date information of the fee, please check the EARL web site under Theranostics certification fees. EARL will send you an invoice via email specifying an invoice number. Please reference the invoice number when transferring the payment.

The accreditation fee needs to be transferred to the following account:
ERSTE Bank
Bank code: 20111
IBAN: AT90 2011 1828 5173 8400
BIC: GIBAATWWXXX

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[1]Mark S. Kaminski, Kenneth R. Zasadny, Isaac R. Francis, Adam W. Milik, Charles W. Ross, Scott D. Moon, Shelley M. Crawford, Jeanne M. Burgess, Neil A. Petry, Gregory M. Butchko, Stephan D. Glenn, and Richard L. Wahl. Radioimmunotherapy of B-cell lymphoma with [131I]anti-B1 (anti-CD20) antibody. N Engl J Med 1993; 329(7): 459-65

[2]Franck Morschhauser 1, John Radford, Achiel Van Hoof, Barbara Botto, Ama Z S Rohatiner, Gilles Salles, Pierre Soubeyran, Herve Tilly, Angelika Bischof-Delaloye, Wim L J van Putten, Jelle W Kylstra, Anton Hagenbeek. ^{90}Yttrium-ibritumomab tiuxetan consolidation of first remission in advanced-stage follicular non-Hodgkin lymphoma: updated results after a median follow-up of 7.3 years from the International, Randomized, Phase III First-LineIndolent trial. J Clin Oncol 2013; 31(16): 1977-83

[3]Mazyar Shadman, Hongli Li, Lisa Rimsza, John P. Leonard, Mark S. Kaminski, Rita M. Braziel, Catherine M. Spier, Ajay K. Gopal, David G. Maloney, Bruce D. Cheson, Shaker Dakhil, Michael LeBlanc, Sonali M. Smith, Richard I. Fisher, Jonathan W. Friedberg, and Oliver W. Press, Continued Excellent Outcomes in Previously Untreated Patients With Follicular Lymphoma After Treatment With CHOP Plus Rituximab or CHOP Plus (131)I-Tositumomab: Long-Term Follow-Up of Phase III Randomized Study SWOG-S0016. J Clin Oncol 2018; 36(7): 697-703

[4]Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedye, Natalie K Rutherford, Andrew Weickhardt, Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, Andrew D Redfern, William Macdonald, Alex Guminski, Edward Hsiao, Wei Chua, Peter Lin, Alison Y Zhang, Margaret M McJannett, Martin R Stockler, John A Violet, Scott G Williams, Andrew J Martin, Ian D Davis "[^{177}Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial," *The Lancet*, vol. 397, no. 10276, pp. 797–804, Feb. 2021, doi: 10.1016/S0140-6736(21)00237-3.

[5]Oliver Sartor, M.D., Johann de Bono, M.B., Ch.B., Ph.D., Kim N. Chi, M.D., Karim Fizazi, M.D., Ph.D., Ken Herrmann, M.D., Kambiz Rahbar, M.D., Scott T. Tagawa, M.D., Luke T. Nordquist, M.D., Nitin Vaishampayan,

M.D., Ghassan El-Haddad, M.D., Chandler H. Park, M.D., Tomasz M. Beer, M.D., Alison Armour, M.B., Ch.B., M.D., Wendy J. Pérez-Contreras, M.P.A., Michelle DeSilvio, Ph.D., Euloge Kpamegan, Ph.D., Germo Gericke, M.D., Ph.D., Richard A. Messmann, M.D., M.H.S., Michael J. Morris, M.D., and Bernd J. Krause, M.D.
, "Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer," *New England Journal of Medicine*, vol. 385, no. 12, pp. 1091–1103, Sep. 2021, doi: 10.1056/NEJMoa2107322.

[6]S. Poty, L. C. Francesconi, M. R. McDevitt, M. J. Morris, and J. S. Lewis, "α-Emitters for Radiotherapy: From Basic Radiochemistry to Clinical Studies-Part 2.," *J Nucl Med*, vol. 59, no. 7, pp. 1020–1027, 2018, doi: 10.2967/jnumed.117.204651

[7]S. Navalkissoor and A. Grossman, "Targeted Alpha Particle Therapy for Neuroendocrine Tumours: The Next Generation of Peptide Receptor Radionuclide Therapy.," *Neuroendocrinology*, vol. 108, no. 3, pp. 256–264, 2019, doi: 10.1159/000494760.

[8]M. G. Ferrier and V. Radchenko, "An Appendix of Radionuclides Used in Targeted Alpha Therapy.," *J Med Imaging Radiat Sci*, vol. 50, no. 4 Suppl 1, pp. S58–S65, 2019, doi: 10.1016/j.jmir.2019.06.051.

[9]Narges K. Tafreshi, Michael L. Doligalski, Christopher J. Tichacek, Darpan N. Pandya, Mikalai M. Budzevich, Ghassan El-Haddad, Nikhil I. Khushalani, Eduardo G. Moros, Mark L. McLaughlin, Thaddeus J. Wadas, and David L. Morse, "Development of Targeted Alpha Particle Therapy for Solid Tumours.," *Molecules*, vol. 24, no. 23, Nov. 2019, doi: 10.3390/molecules24234314.

[10]R. M. de Kruijff, H. T. Wolterbeek, and A. G. Denkova, "A Critical Review of Alpha Radionuclide Therapy-How to Deal with Recoiling Daughters?," *Pharmaceuticals (Basel)*, vol. 8, no. 2, pp. 321–36, Jun. 2015, doi: 10.3390/ph8020321.

[11]C Kratochwil, F L Giesel, F Bruchertseifer, W Mier, C Apostolidis, R Boll, K Murphy, U Haberkorn, A Morgenstern, "[213]Bi-DOTATOC receptor-targeted alpha-radionuclide therapy induces remission in neuroendocrine tumours refractory to beta radiation: a first-in-human experience.," *Eur J Nucl Med Mol Imaging*, vol. 41, no. 11, pp. 2106–19, Nov. 2014, doi: 10.1007/s00259-014-2857-9.

[12]S. Ballal, M. P. Yadav, C. Bal, R. K. Sahoo, and M. Tripathi, "Broadening horizons with [225]Ac-DOTATATE targeted alpha therapy for gastroenteropancreatic neuroendocrine tumour patients stable or refractory to [177]Lu-DOTATATE PRRT: first clinical experience on the efficacy and safety.," *Eur J Nucl Med Mol Imaging*, vol. 47, no. 4, pp. 934–946, 2020, doi: 10.1007/s00259-019-04567-2.

[13]M. A. Kratochwil C, Bruchertseifer F, Giesel F, Apostolidis C, Haberkorn U, "Ac-225-DOTATOC – dose finding for alpha particle emitter based radionuclide therapy of neuroendocrine tumours," *Eur J Nucl Med Mol Imaging*, vol. 42, no. S1, pp. 1–924, Oct. 2015, doi: 10.1007/s00259-015-3198-z.

[14]J. Zhang, H. R. Kulkarni, and R. P. Baum, "Peptide Receptor Radionuclide Therapy Using [225]Ac-DOTATOC Achieves Partial Remission in a Patient With Progressive Neuroendocrine Liver Metastases After Repeated β-Emitter Peptide Receptor Radionuclide Therapy.," *Clin Nucl Med*, vol. 45, no. 3, pp. 241–243, Mar. 2020, doi: 10.1097/RLU.0000000000002915.

[15]S. Ballal, M. P. Yadav, N. A. Damle, R. K. Sahoo, and C. Bal, "Concomitant [177]Lu-DOTATATE and Capecitabine Therapy in Patients With Advanced Neuroendocrine Tumours: A Long-term-Outcome, Toxicity, Survival, and Quality-of-Life Study.," *Clin Nucl Med*, vol. 42, no. 11, pp. e457–e466, Nov. 2017, doi: 10.1097/RLU.0000000000001816.

[16]Clemens Kratochwil, Frank Bruchertseifer, Frederik L Giesel, Mirjam Weis, Frederik A Verburg, Felix Mottaghy, Klaus Kopka, Christos Apostolidis, Uwe Haberkorn, Alfred Morgenstern, "[225]Ac-PSMA-617 for PSMA-Targeted α-Radiation Therapy of Metastatic Castration-Resistant Prostate Cancer.," *J Nucl Med*, vol. 57, no. 12, pp. 1941–1944, Dec. 2016, doi: 10.2967/jnumed.116.178673.

[17]C. Kratochwil *et al.*, "Targeted α-therapy of metastatic castration-resistant prostate cancer with ^{225}Ac-PSMA-617: Dosimetry estimate and empiric dose finding," *Journal of Nuclear Medicine*, vol. 58, no. 10, pp. 1624–1631, Oct. 2017, doi: 10.2967/jnumed.117.191395.

[18]Clemens Kratochwil, Frank Bruchertseifer, Hendrik Rathke, Marcus Bronzel, Christos Apostolidis, Wilko Weichert, Uwe Haberkorn, Frederik L Giesel, Alfred Morgenstern, "Targeted α-Therapy of Metastatic Castration-Resistant Prostate Cancer with ^{225}Ac-PSMA-617: Swimmer-Plot Analysis Suggests Efficacy Regarding Duration of Tumour Control.," *J Nucl Med*, vol. 59, no. 5, pp. 795–802, 2018, doi: 10.2967/jnumed.117.203539.

[19]Mike Sathekge, Frank Bruchertseifer, Otto Knoesen, Florette Reyneke, Ismaheel Lawal, Thabo Lengana, Cindy Davis, Johncy Mahapane, Ceceila Corbett, Mariza Vorster, Alfred Morgenstern, "^{225}Ac-PSMA-617 in chemotherapy-naive patients with advanced prostate cancer: a pilot study.," *Eur J Nucl Med Mol Imaging*, vol. 46, no. 1, pp. 129–138, 2019, doi: 10.1007/s00259-018-4167-0.

[20]Hendrik Rathke, Clemens Kratochwil, Ralph Hohenberger, Frederik Lars Giesel, Frank Bruchertseifer, Paul Flechsig, Alfred Morgenstern, Matti Hein, Peter Plinkert, Uwe Haberkorn, Olcay Cem Bulut, "Initial clinical experience performing sialendoscopy for salivary gland protection in patients undergoing ^{225}Ac-PSMA-617 RLT.," *Eur J Nucl Med Mol Imaging*, vol. 46, no. 1, pp. 139–147, 2019, doi: 10.1007/s00259-018-4135-8.

[21]Mike Sathekge, Frank Bruchertseifer, Mariza Vorster, Ismaheel O Lawal, Otto Knoesen, Johncy Mahapane, Cindy Davis, Florette Reyneke, Alex Maes, Clemens Kratochwil, Thabo Lengana, Frederik L Giesel, Christophe Van de Wiele, Alfred Morgenstern, "Predictors of Overall and Disease-Free Survival in Metastatic Castration-Resistant Prostate Cancer Patients Receiving ^{225}Ac-PSMA-617 Radioligand Therapy.," *J Nucl Med*, vol. 61, no. 1, pp. 62–69, 2020, doi: 10.2967/jnumed.119.229229.

[22]R.L. Tauber, B. Feuerecker, K. Knorr, A. Beheshti, C. Seidl, C. D'Alessandria, F. Bruchertseifer, M. Retz, J.E. Gschwend, W. Weber, A. Morgenstern, M. Eiber, "Safety and efficacy of Ac-225-PSMA-617 in metastatic castration resistant prostate cancer (mCRPC) after failure of Lu-177-PSMA," *Annals of Oncology*, vol. 30, p. v342, Oct. 2019, doi: 10.1093/annonc/mdz248.029.

[23]Fadi Khreish, Niklas Ebert, Martin Ries, Stephan Maus, Florian Rosar, Hendrik Bohnenberger, Tobias Stemler, Matthias Saar, Mark Bartholomä, Samer Ezziddin, "^{225}Ac-PSMA-617/^{177}Lu-PSMA-617 tandem therapy of metastatic castration-resistant prostate cancer: pilot experience.," Eur J Nucl Med Mol Imaging, vol. 47, no. 3, pp. 721–728, 2020, doi: 10.1007/s00259-019-04612-0.

[24]Czernin J, Sonni I, Razmaria A, Calais J. The Future of Nuclear Medicine as an Independent Specialty. Journal of nuclear medicine : official publication, Society of Nuclear Medicine 2019; 60(Suppl 2): 3S-12S.

[25]Claus Zippel, Frederik L Giesel, Clemens Kratochwil, Matthias Eiber, Kambiz Rahbar, Peter Albers, Tobias Maurer, Bernd J Krause, Sabine Bohnet-Joschko, [PSMA radioligand therapy could pose infrastructural challenges for nuclear medicine: results of a basic calculation for the capacity planning of nuclear medicine beds in the German hospital sector.] Nuklearmedizin 2021; 60(3): 216-23.

[26]Avram AM, Giovanella L, Greenspan B, Lawson SA, Luster M, Van Nostrand D, Peacock JG, Ovčariček PP, Silberstein E, Tulchinsky M, Verburg FA, Vrachimis A. SNMMI Procedure Standard/EANM Practice Guideline for Nuclear Medicine Evaluation and Therapy of Differentiated Thyroid Cancer: Abbreviated Version. J Nucl Med. 2022 Jun;63(6):15N-35N. PMID: 35649660.

[27]Alfredo Campennì, Anca M Avram, Frederik A Verburg, Ioannis Iakovou, Heribert Hänscheid, Bart de Keizer, Petra Petranović Ovčariček, Luca Giovanella, The EANM guideline on radioiodine therapy of benign thyroid disease. Eur J Nucl Med Mol Imaging. 2023 Sep;50(11):3324-3348. doi: 10.1007/s00259-023-06274-5. Epub 2023 Jul 3.

[28]Francesco Giammarile, Arturo Chiti, Michael Lassmann, Boudewijn Brans,Glenn Flux, EANM procedure guidelines for [131]I-meta-iodobenzylguanidine ([131]I-mIBG) therapy. *Eur J Nucl Med Mol Imaging* **35**, 1039–1047 (2008). https://doi.org/10.1007/s00259-008-0715-3.

[29]L Bodei, J Mueller-Brand, R P Baum, M E Pavel, D Hörsch, M S O'Dorisio, T M O'Dorisio, J R Howe, M Cremonesi, D J Kwekkeboom, John J Zaknun, The joint IAEA, EANM, and SNMMI practical guidance on peptide receptor radionuclide therapy (PRRNT) in neuroendocrine tumours. *Eur J Nucl Med Mol Imaging* **40**, 800–816 (2013). https://doi.org/10.1007/s00259-012-2330-6.

[30]Clemens Kratochwil, Wolfgang P. Fendler, Matthias Eiber, Michael S. Hofman, Louise Emmett, Jeremie Calais, Joseph R. Osborne, Amir Iravani, Phillip Koo, Liza Lindenberg, Richard P. Baum, Murat Fani Bozkurt, Roberto C. Delgado Bolton, Samer Ezziddin, Flavio Forrer, Rodney J. Hicks, Thomas A. Hope, Levent Kabasakal, Mark Konijnenberg, Klaus Kopka, Michael Lassmann, Felix M. Mottaghy, Wim J. G. Oyen, Kambiz Rahbar, Heiko Schoder, Irene Virgolini, Lisa Bodei, Stefano Fanti, Uwe Haberkorn & Ken Hermann, Joint EANM/SNMMI procedure guideline for the use of [177]Lu-labeled PSMA-targeted radioligand-therapy ([177]Lu-PSMA-RLT). *Eur J Nucl Med Mol Imaging* **50**, 2830–2845 (2023). https://doi.org/10.1007/s00259-023-06255-8

[31]Radiation Protection and Safety of Radiation Sources: International Basic Safety Standards. Vienna: INTERNATIONAL ATOMIC ENERGY AGENCY; 2014.

[32]The 2007 Recommendations of the International Commission on Radiological Protection. ICRP publication 103. Ann ICRP 2007; 37(2-4): 1-332.

[33]Council of the European Union. COUNCIL DIRECTIVE 2013/59/EURATOM of 5 December 2013 laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation, and repealing Directives 89/618/Euratom, 90/641/Euratom, 96/29/Euratom, 97/43/Euratom and 2003/122/Euratom. Official Journal of the EU 2014; L13: 1-73.

[34]ICRP Publication 105. Radiation protection in medicine. Ann ICRP 2007; 37(6): 1-63

[35]R Gadd, M Baker, K S Nijran, S Owens, W Thomson, M J Woods, F Zananiri, Protocol for Establishing and Maintaining the Calibration of Medical Radionuclide Calibrators and their Quality Control, 2006

[36]AAPM. The selection, use, calibration and quality assurance of radionuclide calibrators used in nuclear medicine: American Association of Physicist in Medicine, 2012.

[37]IAEA. Quality assurance for radioactivity measurement in nuclear medicine. Vienna: Internation Atomic Energy Agency, 2006

[38]EANM Physics Committee; Busemann Sokole E, Płachcínska A, Britten A; EANM Working Group on Nuclear Medicine Instrumentation Quality Control; Lyra Georgosopoulou M, Tindale W, Klett R, Routine quality control recommendations for nuclear medicine instrumentation. Eur J Nucl Med Mol Imaging 2010; 37(3): 662-71.

[39]Busemann Sokole E, Plachcinska A, Britten A, Committee EP. Acceptance testing for nuclear medicine instrumentation. Eur J Nucl Med Mol Imaging 2010; 37(3): 672-81.

[40]IAEA. Quality assurance for radioactivity measurement in nuclear medicine. Vienna: Internation Atomic Energy Agency, 2006