

BÖLÜM

4

RADYOKILAVUZLU CERRAHİ UYGULAMALARINDA KULLANILAN RADYOFARMASÖTİKLER

Fadime DEMİR¹

GİRİŞ

Cerrahi uygulamalara yardımcı nükleer tıp yöntemleri son dönemde kullanımını giderek artan, gereksiz cerrahi uygulamalardan kaçınmayı sağlayan ve tedavi yöntem seçimine yardımcı olan uygulamalardır. Radyokılavuzlu cerrahi uygulamalarının tarihçesi 1949 yılında Selverstone ve arkadaşlarının beyin tümörlerinin cerrahisinde Fosfor-32 (P-32) ve Geiger-Müller cihazı kullanarak yaptıkları çalışmaya kadar uzanmaktadır (1). Uygulamaları üç başlık altında toplamak mümkündür. Bunlar 1) Sentinel Lenf Nodu (SLN) Görüntülemesi ve radyokılavuzlu cerrahisi 2) Radyasyon kılavuzluğunda küçük lezyon lokalizasyonu yöntemi olan RKLL ve radyoaktif çekirdek (seed) ile işaretleme yöntemi olan RÇİ uygulamaları (direkt yöntem) ve 3) Radyasyon kılavuzluğunda cerrahi uygulamalar (indirekt yöntem)'dir.

SENTİNEL LENF NODU (SLN) GÖRÜNTÜLEMESİ VE RADYOKILAVUZLU CERRAHİSİ

Sentinel lenf nodu primer tümörün doğrudan direne olduğu bölgesel lenf düğümleri olup, metastatik hücrelerin lenfatik yolla var olabileceği ilk bölgedir. SLN haritalaması ve biyopsisi erken evre tümörlerde lenfatik yayılım olup olmadığının saptanmasını sağlayarak, daha az invaziv cerrahi prosedürlerin uy-

¹ Dr. Öğr. Üyesi, Tokat Gaziosmanpaşa Üniversitesi, drfadimedemir@hotmail.com

çalışmada uygun maliyet ve üstün performansı nedeniyle potansiyeli yüksek bir ajan olarak sunulmuştur (79). Maurer ve arkadaşlarının yapmış olduğu çalışmada Ga-68-PSMA PET/BT görüntülemesinin ardından ortalama 571 MBq (15 mCi) Tc-99m-PSMA (Tc-99m-PSMA-I&S) enjeksiyonundan bir sonraki gün (ortalama 19,7 saat) uygulanan cerrahi ile metastatik lezyonların başarılı bir şekilde çıkarıldığı raporlanmıştır (80).

SONUÇ

Cerrahi uygulamalarda temel alınan amaçlar etkinlik, cerrahi süresinin minimumda tutmak ve hastanın en kısa sürede hastaneden taburcu olmasını sağlayarak maliyetin azaltılmasıdır. Radyokılavuzlu cerrahi uygulamalar cerrahi uygulanacak lezyonun kolay ve doğru biçimde lokalizasyonunu sağlarken, diğer yandanda cerrahi kesi alanının minimuma indirilmesine yardımcı olmakta böylece operasyon süresini azaltmaktadır. Son yıllarda artan bir ivmeyle alanında bir çok gelişme ve yenilik izlenen nükleer tıp yöntemleri ve radyonüklidler, klinisyenlere tanı ve tedavi alanında yardımlarının yanı sıra, cerrahi alanda da giderek artan kullanım ve etkinlik sağlayacağını düşündürmektedir.

KAYNAKLAR

1. Selverstone B, Sweet WH, Robinson CV. The clinical use of radioactive phosphorus in the surgery of brain tumors. *Ann Surg.* 1949; 130 (4): 643-651.
2. Moncayo V, Grady EE, Alazraki NP, et al. Sentinel-Lymph-Node Multicenter Trials. *Semin Nucl Med.* 2020; 50(1): 56-74. doi: 10.1053/j.semnuclmed.2019.10.001
3. Veronesi U, Paganelli G, Galimberti V, et al. Sentinel node biopsy to avoid AD in breast cancer with clinically negative lymph-nodes. *Lancet.* 1997; 349(9069):1864-1867. doi:10.1016/S0140-6736(97)01004-0.
4. Giammarile F, Alazraki N, Aarsvold JN, et al. The EANM and SNMMI practice guideline for lymphoscintigraphy and sentinel node localization in breast cancer. *Eur J Nucl Med Mol Imaging.* 2013; 40(12):1932-1947. doi: 10.1007/s00259-013-2544-2.
5. Quartuccio N, Siracusa M, Pappalardo M, et al. Sentinel Node Identification in melanoma: current clinical impact, new emerging SPECT radiotracers and technological advancements. An update of the last decade. *Curr Radiopharm.* 2020; 13(1): 32-41. doi: 10.2174/1874471012666191015100837.
6. Tsopelas C. Particle size analysis of (99m) Tc-labeled and unlabeled antimony trisulfide and rhenium sulfide colloids intended for lymphoscintigraphic application. *J Nucl Med.* 2001; 42(3):460-466.

7. Tu W, Denizot B. Synthesis of small-sized rhenium sulfide colloidal nanoparticles. *Journal of Colloid and Interface Science*. 2007; 310 (1):167-170. doi: 10.1016/j.jcis.2007.01.054.
8. Bensimhon L, Métafé T, Guilhot J, et al. Influence of temperature on the radiochemical purity of Tc-99m-colloidal rhenium sulfide for use in sentinel node localization. *Nucl Med Commun*. 2008; 29 (11):1015–1020. doi: 10.1097/MNM.0b013e-32830ebd13.
9. Subramanian S, Pandey U, Shah S, et al. An indigenous single-vial kit formulation of human serum albumin nanocolloid for use in sentinel lymph node detection. *Nucl Med Commun*. 2015; 36 (8):848–853. doi: 10.1097/MNM.0000000000000333.
10. Jimenez IR, Roca M, Vega E, et al. Particle sizes of colloids to be used in sentinel lymph node radiolocalization. *Nucl Med Commun*. 2008; 2(2):166–172. doi: 10.1097/MNM.0b013e3282f258d9.
11. Hill AD, Tran KN, Yeung H, et al. Sentinel lymph node biopsy in breast cancer: unfiltered radioisotope is superior to filtered. *J Am Coll Surg*. 1999; 188(4):377–381. doi: 10.1016/s1072-7515(98)00314-7.
12. Cody HS 3rd, Borgen PI. State-of-the-art approaches to sentinel node biopsy for breast cancer: study design, patient selection, technique, and quality control at Memorial Sloan-Kettering Cancer Center. *Surg Oncol*, 1999; 8(2):85-91. doi: 10.1016/s0960-7404(99)00029-8.
13. Nelson KP, Choudhury KR, Coleman RE, et al. Does the preparation and utilization of Tc-99m-sulfur colloid affect the outcomes of breast lymphoscintigraphy? *J Nucl Med Technol*. 2013; 41(2):92-98. doi: 10.2967/jnmt.112.117820.
14. Tokin CA, Cope FO, Metz WL, et al. The efficacy of Tilmanocept in sentinel lymph node mapping and identification in breast cancer patients: a comparative review and meta-analysis of the ^{99m}Tc-labeled nanocolloid human serum albumin standard of care. *Clin Exp Metastasis*. 2012; 29(7):681-6. doi: 10.1007/s10585-012-9497-x.
15. Mariani G, Moresco L, Viale G, et al. Radioguided sentinel lymph node biopsy in breast cancer surgery. *J Nucl Med*. 2001; 42(8):1198–1215.
16. Huang YY, Maurel A, Hamza S, et al. Impact of same day vs day before pre-operative lymphoscintigraphy for sentinel lymph node biopsy for early breast cancer (local Australian experience). *J Med Imaging Radiat Oncol*. 2018; 62(3):320-323. doi: 10.1111/1754-9485.12689.
17. Unkart JT, Baker JL, Hosseini A, et al. Comparison of Post-injection Site Pain Between Technetium Sulfur Colloid and Technetium Tilmanocept in Breast Cancer Patients Undergoing Sentinel Lymph Node Biopsy. *Ann Surg Oncol*. 2015; 22 Suppl 3: S559–S565. doi: 10.1245/s10434-015-4802-y.
18. Wallace AM, Hoh CK, Ellner SJ, Darrah DD, Schulteis G, Vera DR. Lymphoseek: a molecular imaging agent for melanoma sentinel lymph node mapping. *Ann Surg Oncol*. 2007; 14(2):913-921. doi: 10.1245/s10434-006-9099-4.
19. Kim EM, Lim ST, Sohn MH, Jeong HJ. Size Control of (99m)Tc-tin Colloid Using PVP and Buffer Solution for Sentinel Lymph Node Detection. *J Korean Med Sci*. 2015; 30(6):816–822. doi: 10.3346/jkms.2015.30.6.816.

20. Wang G, Wu E, Wang Y, Huang H, Zhou Y, Chen Z. The synthesis of a new macromolecule for the sentinel node detection: Tc-99m-gly-mannosyl-dextran. *Nucl Med Commun.* 2019; 40(2):131–135. doi: 10.1097/MNM.0000000000000951.
21. Manca G, Mazzarri S, Rubello D, et al. Radioguided Occult Lesion Localization: Technical Procedures and Clinical Applications. *Clin Nucl Med.* 2017; 42(12): e498–e503. doi: 10.1097/RLU.0000000000001858.
22. Bozkurt MF. Sentinel Lymph Node Imaging and Lymphatic Mapping. *Nuclear Medicine Seminars / Nükleer Tıp Seminerleri.* 2016; 2 (1):42-48.
23. Povoski SP, Neff RL, Mojzsisik CM, et al. A comprehensive overview of radioguided surgery using gama detection probe technology. *World J Surg Oncol.* 2009; 7:11. doi: 10.1186/1477-7819-7-11.
24. International Atomic Energy Agency (IAEA), ed. Guided Intraoperative Scintigraphic Tumour Targeting (GOSTT): Implementing advanced hybrid molecular imaging and non-imaging probes for advanced cancer management. IAEA HUMAN HEALTH SERIES No. 29, Vienna, 2014.
25. Deepak J, Mandeep Singh M. Radioguided occult lesion localization and sentinel node and occult lesion localization in breast cancer, the future beckons. *Asian J Oncol.* 2015; 1 (2): 73-6. doi: 10.4103/2454-6798.173283.
26. Sheetz M, Steiner C. Compliance with the U.S. Nuclear Regulatory Commission Revised Licensing Guidance for Radioactive Seed Localization. *Health Phys.* 2018; 115(3):402–408. doi: 10.1097/HP.0000000000000889.
27. Gray RJ, Salud C, Nguyen K, et al. Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization. *Ann Surg Oncol.* 2001; 8(9):711–715. doi: 10.1007/s10434-001-0711-3.
28. Stelle L, Schoenheit T, Brubaker A, et al. Radioactive Seed Localization Versus Wire Localization for Nonpalpable Breast Lesions: A Two-Year Initial Experience at a Large Community Hospital. *Ann Surg Oncol.* 2018; 25(1):131–136. doi: 10.1245/s10434-017-6102-1.
29. Hassing CM, Tvedskov TF, Kroman N, et al. Radioactive seed localization of renal cell carcinoma in a patient with Von Hippel-Lindau disease. *Clin Case Rep.* 2016; 5(1):26–28. doi: 10.1002/ccr3.685.
30. Wang GL, Tsikouras P, Zuo HQ, et al. Radioactive seed localization and wire guided localization in breast cancer: A systematic review and meta-analysis. *J BUON.* 2019; 24(1):48–60.
31. Sánchez R, González Jiménez AD, Rebollo Aguirre AC, et al. ¹⁻¹²⁵ radioactive seed localization for non-palpable lesions in breast cancer. Semillas de ¹⁻¹²⁵ en la localización de lesiones no palpables en pacientes con cáncer de mama. *Rev Esp Med Nucl Imagen Mol.* 2019; 38(6):343–347.
32. Noureldine SI, Gooi Z, Tufano RP. Minimally invasive parathyroid surgery. *Gland Surg.* 2015; 4(5):410–419. doi: 10.3978/j.issn.2227-684X.2015.03.07.
33. Gültekin SS, Saylam G, Delibaşı T, et al. The contributions of gama probe to lesion detectability and surgical safety in recurrent thyroid cancer at risk. *Mol Imaging Radionucl Ther.* 2013; 22(2):56–59. doi: 10.4274/Mirt.148.

34. Pashazadeh A, Friebe M. Radioguided surgery: physical principles and an update on technological developments. *Biomed Tech (Berl)*. 2020;65(1):1-10. doi: 10.1515/bmt-2018-0016.
35. Howe JR. Radioguided Surgery With Gallium for Neuroendocrine Tumors. *JAMA Surg*. 2019; 154(1):45-46. doi: 10.1001/jamasurg.2018.3480.
36. Cuccurullo V, Di Stasio GD, Mansi L. Radioguided surgery with radiolabeled somatostatin analogs: not only in GEP-NETs. *Nucl Med Rev Cent East Eur*. 2017; 20(1):49-56. doi: 10.5603/NMR.2017.0003.
37. Knipper S, Tilki D, Mansholt J, et al. Metastases-yield and Prostate-specific Antigen Kinetics Following Salvage Lymph Node Dissection for Prostate Cancer: A Comparison Between Conventional Surgical Approach and Prostate-specific Membrane Antigen-radioguided Surgery. *Eur Urol Focus*. 2019; 5(1):50-53. doi: 10.1016/j.euf.2018.09.014.
38. Kratzik C, Dorudi S, Schatzl M, et al. Tc-99m-PSMA imaging allows successful radioguided surgery in recurrent prostate cancer. *Hell J Nucl Med*. 2018; 21(3):202-204. doi: 10.1967/s002449910906.
39. Horn T, Krönke M, Rauscher I, et al. Single Lesion on Prostate-specific Membrane Antigen-ligand Positron Emission Tomography and Low Prostate-specific Antigen Are Prognostic Factors for a Favorable Biochemical Response to Prostate-specific Membrane Antigen-targeted Radioguided Surgery in Recurrent Prostate Cancer. *Eur Urol*. 2019; 76(4):517-523. doi: 10.1016/j.eururo.2019.03.045.
40. Collamati F, Bocci V, Castellucci P, et al. Radioguided surgery with β radiation: a novel application with Ga-68. *Sci Rep*. 2018; 8(1):16171. doi: 10.1038/s41598-018-34626-x.
41. Madeddu G, Spanu A. Use of tomographic nuclear medicine procedures, SPECT and pinhole SPECT, with cationic lipophilic radiotracers for the evaluation of axillary lymph node status in breast cancer patients. *Eur J Nucl Med Mol Imaging*. 2004; 31 Suppl 1: S23-S34. doi: 10.1007/s00259-004-1524-y.
42. Botushanova AD, Botushanov NP, Yaneva MP. Nuclear Medicine Methods for Evaluation of Abnormal Parathyroid Glands in Patients with Primary and Secondary Hyperparathyroidism. *Folia Med (Plovdiv)*. 2017; 59(4):396-404. doi: 10.1515/fol-med-2017-0054.
43. Denmeade KA, Constable C, Reed WM. Use of (99m) Tc 2-methoxyisobutyl isonitrite in minimally invasive radioguided surgery in patients with primary hyperparathyroidism: A narrative review of the current literature. *J Med Radiat Sci*. 2013; 60(2):58-66. doi: 10.1002/jmrs.14.
44. Friedman M, Gurpinar B, Schalch P, et al. Guidelines for radioguided parathyroid surgery. *Arch Otolaryngol Head Neck Surg*. 2007; 133(12):1235-1239. doi: 10.1001/archotol.133.12.1235
45. Valdés Olmos RA, Vidal-Sicart S, Manca G, et al. Advances in radioguided surgery in oncology. *Q J Nucl Med Mol Imaging*. 2017; 61(3):247-270. doi: 10.23736/S1824-4785.17.02995-8
46. Casara D, Rubello D, Saladini G, et al. Clinical approach in patients with differentiated thyroid carcinoma and negative ^{131}I whole body scintigraphy: importance of Tc-99m-MIBI scan combined with high resolution neck ultrasonography. *Tumori*, 1999; 85(2):122-127.

47. Chapman GJ, Povoski SP, Hall NC, et al. Comparison of two threshold detection criteria methodologies for determination of probe positivity for intraoperative in situ identification of presumed abnormal F-18-FDG-avid tissue sites during radioguided oncologic surgery. *BMC Cancer*. 2014; 14:667. doi: 10.1186/1471-2407-14-667.
48. Povoski SP, Sarikaya I, White WC, et al. Comprehensive evaluation of occupational radiation exposure to intraoperative and perioperative personnel from F-18-FDG radioguided surgical procedures. *Eur J Nucl Med Mol Imaging*. 2008; 35(11):2026–2034. doi: 10.1007/s00259-008-0880-4.
49. Meller B, Sommer K, Gerl J, et al. High energy probe for detecting lymph node metastases with F-18-FDG in patients with head and neck cancer. *Nuklearmedizin*. 2006; 45(4):153–159.
50. Meller B, Sahlmann C, Horstmann O, et al. Conventional gama and high energy probe for radioguided dissection of metastases in a patient with recurrent thyroid carcinoma with (99m) Tc-MIBI and (18)F-FDG. *Nuklearmedizin*. 2005; 44(3): N23–N25.
51. Curtet C, Carlier T, Mirallié E, et al. Prospective comparison of two gama probes for intraoperative detection of F-18-FDG: in vitro assessment and clinical evaluation in differentiated thyroid cancer patients with iodine-negative recurrence. *Eur J Nucl Med Mol Imaging*. 2007; 34(10):1556–1562. doi: 10.1007/s00259-007-0393-6.
52. Povoski SP, Hall NC, Murrey DA Jr, et al. Multimodal imaging and detection approach to F-18-FDG-directed surgery for patients with known or suspected malignancies: a comprehensive description of the specific methodology utilized in a single-institution cumulative retrospective experience. *World J Surg Oncol*. 2011; 9:152. doi: 10.1186/1477-7819-9-152.
53. Ivanidze J, Roytman M, Sasson A, et al. Molecular imaging and therapy of somatostatin receptor positive tumors. *Clin Imaging*. 2019; 56:146–154. doi: 10.1016/j.clinimag.2019.04.006.
54. Fani M, Nicolas GP, Wild D. Somatostatin Receptor Antagonists for Imaging and Therapy. *J Nucl Med*. 2017; 58(Suppl 2):61S–66S. doi: 10.2967/jnumed.116.186783.
55. Kaemmerer D, Prasad V, Daffner W, et al. Radioguided surgery in neuroendocrine tumors using Ga-68-labeled somatostatin analogs: a pilot study. *Clin Nucl Med*. 2012; 37(2):142–147. doi: 10.1097/RLU.0b013e3182291de8.
56. Hubalewska-Dydejczyk A, Kulig J, Szybinski P, et al. Radio-guided surgery with the use of [Tc-99m-EDDA/HYNIC]octreotate in intra-operative detection of neuroendocrine tumours of the gastrointestinal tract. *Eur J Nucl Med Mol Imaging*. 2007; 34(10):1545–1555. doi: 10.1007/s00259-007-0476-4.
57. Trogrlic M, Tezak S. Tc-99m-EDDA/HYNIC-TOC in management of patients with head and neck somatostatin receptor positive tumors. *Nucl Med Rev Cent East Eur*. 2016; 19(2):74–80. doi: 10.5603/NMR.2016.0016.
58. Sharp SE, Trout AT, Weiss BD, Gelfand MJ. MIBG in Neuroblastoma Diagnostic Imaging and Therapy. *Radiographics*. 2016; 36(1):258–278. doi: 10.1148/rg.2016150099.
59. Van Hulsteijn LT, Corssmit EP, van der Hiel B, et al. Is there a role for radioguided surgery with iodine-labeled metaiodobenzylguanidine in resection of neuroendocrine tumors? *Clin Nucl Med*. 2012; 37(11):1083–1088. doi: 10.1097/RLU.0b013e318266cb3d.

60. Martelli H, Ricard M, Larroquet M, et al. Intraoperative localization of neuroblastoma in children with I-123- or I-125-radiolabeled metaiodobenzylguanidine. *Surgery*. 1998; 123(1):51–57.
61. Buhl T, Mortensen J, Kjaer A. I-123 MIBG imaging and intraoperative localization of metastatic pheochromocytoma: a case report. *Clin Nucl Med*. 2002; 27(3):183–185. doi: 10.1097/00003072-200203000-00007.
62. Adams S, Acker P, Lorenz M, et al. Radioisotope-guided surgery in patients with pheochromocytoma and recurrent medullary thyroid carcinoma: a comparison of preoperative and intraoperative tumor localization with histopathologic findings. *Cancer*. 2001; 92(2):263–270. doi: 10.1002/1097-0142(20010715)92:2<263::aid-cncr1318>3.0.co;2-z.
63. Lamberts SWJ, Hofland LJ. ANNIVERSARY REVIEW: Octreotide, 40 years later. *Eur J Endocrinol*. 2019; 181(5): R173–R183. doi: 10.1530/EJE-19-0074.
64. Martinez DA, O'Dorisio MS, O'Dorisio TM, et al. Intraoperative detection and resection of occult neuroblastoma: a technique exploiting somatostatin receptor expression. *J Pediatr Surg*. 1995; 30(11):1580–1589. doi: 10.1016/0022-3468(95)90161-2.
65. Schirmer WJ, O'Dorisio TM, Schirmer TP, et al. Intraoperative localization of neuroendocrine tumors with I-125-TYR(3)-octreotide and a hand-held gama-detecting probe. *Surgery*. 1993; 114(4):745–752.
66. Critchley M. Octreotide scanning for carcinoid tumours. *Postgrad Med J*. 1997; 73(861):399–402. doi: 10.1136/pgmj.73.861.399.
67. Chatal JF, Perkins AC, Baum RP, et al. The long history of the International Research Group in Immuno-Scintigraphy and Therapy (IRIST). *Q J Nucl Med Mol Imaging*. 2015; 59(2):137–139.
68. Krenning EP, Kwekkeboom DJ, Bakker WH, et al. Somatostatin receptor scintigraphy with [In-111-DTPA-D-Phe1]- and [I-123-Tyr3]-octreotide: the Rotterdam experience with more than 1000 patients. *Eur J Nucl Med*. 1993; 20(8):716–731. doi: 10.1007/BF00181765.
69. Olsen JO, Pozderac RV, Hinkle G, et al. Somatostatin receptor imaging of neuroendocrine tumors with indium-111 pentetreotide (Octreoscan). *Semin Nucl Med*. 1995; 25(3):251–261. doi: 10.1016/s0001-2998(95)80014-x.
70. Ohrvall U, Westlin JE, Nilsson S, et al. Intraoperative gama detection reveals abdominal endocrine tumors more efficiently than somatostatin receptor scintigraphy. *Cancer*. 1997; 80(12 Suppl):2490–2494. doi: 10.1002/(sici)1097-0142(19971215)80:12+<2490::aid-cncr21>3.3.co;2-t.
71. Wang YZ, Diebold A, Woltering E, et al. Radioguided exploration facilitates surgical cytoreduction of neuroendocrine tumors. *J Gastrointest Surg*. 2012; 16(3):635–640. doi: 10.1007/s11605-011-1767-4.
72. Lupold SE. Aptamers and apple pies: a mini-review of PSMA aptamers and lessons from Donald S. Coffey. *Am J Clin Exp Urol*. 2018; 6(2):78–86.
73. Barrio M, Fendler WP, Czernin J, et al. Prostate specific membrane antigen (PSMA) ligands for diagnosis and therapy of prostate cancer. *Expert Rev Mol Diagn*. 2016; 16(11):1177–1188. doi: 10.1080/14737159.2016.1243057.

74. Mix M, Reichel K, Stoykow C, et al. Performance of ^{111}In -labelled PSMA ligand in patients with nodal metastatic prostate cancer: correlation between tracer uptake and histopathology from lymphadenectomy. *Eur J Nucl Med Mol Imaging*. 2018; 45(12):2062–2070. doi: 10.1007/s00259-018-4094-0.
75. Derks YHW, Löwik DWPM, Sedelaar JPM, et al. PSMA-targeting agents for radio- and fluorescence-guided prostate cancer surgery. *Theranostics*. 2019; 9(23):6824–6839. doi: 10.7150/thno.36739.
76. Rauscher I, Düwel C, Wirtz M, et al. Value of ^{111}In -prostate-specific membrane antigen (PSMA)-radioguided surgery for salvage lymphadenectomy in recurrent prostate cancer: correlation with histopathology and clinical follow-up. *BJU Int*. 2017; 120(1):40–47. doi: 10.1111/bju.13713.
77. Shetty D, Lee YS, Jeong JM. ^{68}Ga -Labeled Radiopharmaceuticals for Positron Emission Tomography. *Nucl Med Mol Imaging*. 2010; 44 (4):233–240. doi: 10.1007/s13139-010-0056-6.
78. Schwarzenboeck SM, Rauscher I, Bluemel C, et al. PSMA Ligands for PET Imaging of Prostate Cancer [published correction appears in *J Nucl Med*. 2017 Nov;58(11):1881]. *J Nucl Med*. 2017; 58(10):1545–1552. doi: 10.2967/jnumed.117.191031.
79. Robu S, Schottelius M, Eiber M, et al. Preclinical Evaluation and First Patient Application of $^{99\text{m}}\text{Tc}$ -PSMA-I&S for SPECT Imaging and Radioguided Surgery in Prostate Cancer. *J Nucl Med*. 2017; 58(2):235–242. doi: 10.2967/jnumed.116.178939.
80. Maurer T, Robu S, Schottelius M, et al. $^{99\text{m}}\text{Tc}$ -based Prostate-specific Membrane Antigen-radioguided Surgery in Recurrent Prostate Cancer. *Eur Urol*. 2019; 75(4):659–666. doi: 10.1016/j.eururo.2018.03.013.