

Bölüm 11

GASTROENTEROPANKREATİK NÖROENDOKRİN TÜMÖRLERDE RADYOLOJİK İNCELEMELER VE TEDAVİDE GİRİŞİMSEL RADYOLOJİ

Aysun ERBAHÇECİ SALIK¹²

GİRİŞ

Diffüz endokrin sisteme ait birbirinden farklı fonksiyonlara sahip ve farklı hormonlar üreten özelleşmiş hücrelerden köken alan ve gelişen nöroendokrin tümörler (NET) bu özelliklerinden dolayı çok çeşitli klinik tablolar ile karşımıza çıkabilirler. Bununla birlikte NET görüntüleme yöntemlerinin uygulanmasına temel oluşturan bazı özgün özelliklere de sahiptir. Son 4 dekatta giderek artış bildirilen insidansları güncel olarak 3,0-5,2/100000 olarak tahmin edilmektedir, prevalansları ise 35/100000 olarak hesaplanmaktadır (1,2). NET'ler en sık gastro-intestinal ve bronkopuloner sistemde bulunurlar (3).

NET'ler fonksiyonel olup metabolik olarak aktif hormonlar veya aminler salgılayabilir ve buna bağlı klinik semptomlara sebep olabilirler veya non fonksiyone olabilirler ve bu durumda da sıklıkla lokal ileri evre hastalık ya da metastazlar ile prezente olurlar (4,5). Örneğin gastroenteropankreatik NET'lerden (GEP-NET) ince barsak NET'leri genelde serotonin salgılayan, fonksiyonel pankreatik NET'ler köken aldıkları langerhans hücresine göre farklı hormonlar (insülin, glukagon, gastrin vb) salgılayabilirler. NET'lerin çok büyük bir kısmı yavaş büyürler ve somatostatin reseptörleri eksprese ederler ki bu da fonksiyonel görüntülemenin temelini oluşturur (ki-67 indeks \leq %2, G1). Diğer küçük bir kısmı ise daha yüksek proliferasyon indeksi ile daha hızlı büyürler ve klinik olarak daha agresif davranırlar (ki-67 indeks: %3-20, G2). Nadiren de kötü diferansiyasyon gösteren, yüksek proliferasyon indeksli nöroendokrin karsinomlar (ki67 indeks $>$ %20, G3) görülebilir. Bu farklı klinik tablolar nedeniyle de herbir hastada ihtiyaç duyulan görüntüleme yöntemi de farklılıklar göstermektedir.

¹² Dr. Aysun Erbahçeci İstanbul Sağlık Bilimleri Üniversitesi Bakırköy Dr. Sadi Konuk EAH
aysunerbahceci@yahoo.com

ampulla düzeyinde koledokta bası oluşturan yaklaşık 1 cm boyutlu, arteriyel fazda daha belirgin olmak üzere kontrastlanma gösteren lezyon izlenmektedir. Bu lezyonun patoloji sonucu NET olarak gelmiştir.

Resim 7 74 y karın ağrısı semptomu ile başvuran K hastada kontrastlı BT tetkikinde aksiyel ve koronal rekonstrüksiyon imajlarında ileal ans komşuluğunda santral nekrotik dejenerasyon gösteren, heterojen kontrastlanan büyük boyutlu lezyon izlenmiştir. Bu lezyon tespit edildikten sonra opere olan hastada lezyonun komşu ileal ans ile yapışık olduğu görülmüş ve ileal ans içerisinde milimetrik boyutlu NET histopatolojik olarak tespit edilmiştir.

Resim 8: 67 y K hasta akut appendisit şüphesi ve kliniği nedeniyle çekilen kontrastlı abdomen BT'de çekum duvarında da kalılaşmaya yol açan appendiksin tamamını tutan lezyon izlenmektedir. Postop histopatoloji sonucunda bu lezyonun appendiksi tutan NET olduğu raporlanmıştır. Resim 9 84 y K hastada genel durum bozukluğu nedeniyle yapılan tetkiklerinde BT incelemede rektum duvarında duvar kalınlaşması ve karaciğerde arteriyel fazda (b) hafif heterojen kontrastlanmaya başlayan ve portal venöz fazda (c) karaciğer parankimal fazı oluşturulan sonra hipodens hipovasküler multiple lezyon izlenmiştir. Hastanın karaciğer kitle biyopsi sonucu NET ile uyumlu gelmiş ve rektum duvarından alınan biyopsi tanıyı rektum NET olarak kesinleştirmiştir. Resim 10 52 y K hasta karaciğerde multiple primer GIS NET'e sekonder metastazları mevcut (a,b), transarteriyel kemoembolizasyon uygulanan hastada işlem öncesinde alınan anjiyografide hipervasküler lezyonlar izlenirken, embolizasyon sonrasında lezyonlarda vaskülaritenin tama yakın kaybolduğunu görülmektedir (c,d).

KAYNAKLAR

1. Yao JC, Hassan M, Phan A, et al. One hundred years after "Carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *J Clin Oncol* 2008;26(18):3063-3072
2. Oberg K, Akerström G, Rindi G, Jelic S; ESMO Guidelines Working Group. Neuroendocrine gastroenteropancreatic tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2010;21(Suppl 5):v223-v227
3. Sundin A. Radiological and nuclear medicine imaging of gastroenteropancreatic neuroendocrine tumors. *Best Pract Res Clin Gastroenterol*. 2012 Dec;26(6):803-18.
4. Turaga KK, Kvols LK. Recent progress in the understanding, diagnosis, and treatment of gastroenteropancreatic neuroendocrine tumors. *CA Cancer J Clin* 2011;61(2):113-132.
5. Sundin A, Vullierme MP, Kaltsas G, Plöckinger U; Mallorca Consensus Conference participants; European Neuroendocrine Tumor Society. ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: radiological examinations. *Neuroendocrinology* 2009;90(2):167-183.
6. Lawrence B, Gustafsson BI, Chan A, Svejda B, Kidd M, Modlin IM. The epidemiology of gast-

- roenteropancreatic neuroendocrine tumors. *Endocrinol Metab Clin North Am* 2011;40(1):1-18.
7. Yu R, Wachsman A. Imaging of neuroendocrine tumors: indications, interpretations, limits and pitfalls. *Endocrinol Metab Clin N Am* 2017;46:795-814.
 8. Thakker RV, Newey PJ, Walls GV, et al. Clinical Practice Guidelines for multiple endocrine neoplasia type 1 (MEN1). *J Clin Endocrinol Metab* 2012;97:2990-3011.
 9. Steward MJ1, Warbey VS, Malhotra A, Caplin ME, Buscombe JR, Yu D. Neuroendocrine tumors: role of interventional radiology in therapy. *Radiographics*. 2008 Jul-Aug;28(4):1131-45.
 10. Tan EH, Tan CH. Imaging of gastroenteropancreatic neuroendocrine tumors. *World J Clin Oncol* 2011;2(1):28-43
 11. Tamm EP, Kim EE, Ng CS. Imaging of neuroendocrine tumors. *Hematol Oncol Clin North Am* 2007;21(3):409-432.
 12. Dumortier J, Ratineau C, Roche C, Lombard-Bohas C, Chayvialle JA, Scoazec JY. Angiogenesis and endocrine tumors. *Bull Cancer* 1999;86(2):148-153.
 13. Procacci C, Carbognin G, Accordini S et al. Nonfunctioning endocrine tumors of the pancreas: possibilities of spiral CT characterization. *Eur Radiol* 2001;11(7):1175-1183
 14. Herwick S, Miller Fh, Keppke AL. MRI of islet cell tumors of the pancreas. *AJR Am J Roentgenol* 2006;187(5):W472-W480.
 15. Ichikawa T, Peterson MS, Federle MP, et al. Islet cell tumor of the pancreas: biphasic CT versus MR imaging in tumor detection. *Radiology* 2000;216(1):163-171.
 16. Kamaoui I, De-Luca V, Ficarella S, Mennesson N, Lombard-Bohas C, Pilleul F. Value of CT enteroclysis in suspected small-bowel carcinoid tumors. *AJR Am J Roentgenol* 2010;194(3):629-633.
 17. Ilangovan R, Burling D, George A, et al. CT enterography: review of technique and practical tips. *Br J Radiol* 2012;85:876-86
 18. Woodard PK, Feldman JM, Paine SS, Baker ME. Midgut carcinoid tumors: CT findings and biochemical profiles. *J Comput Assist Tomogr* 1995;19(3):400-405.
 19. Fletcher JG, Kofler JM, Coburn JA, et al. Perspective on radiation risk in CT imaging. *Abdom Imaging* 2013;38:22-31.
 20. Dromain C, de Baere T, Lumbroso J, et al. Detection of liver metastases from endocrine tumors: a prospective comparison of somatostatin receptor scintigraphy, computed tomography, and magnetic resonance imaging. *J Clin Oncol* 2005;23:70-8.
 21. Giesel FL, Kratochwil C, Mehndiratta A, Wulfert S, Moltz JH, Zechmann CM, et al. Comparison of neuroendocrine tumor detection and characterization using DOTATOC-PET in correlation with contrast enhanced CT and delayed contrast enhanced MRI. *Eur J Radiol* 2012;81:2820-5.
 22. Bader TR, Semelka RC, Chiu VC, Armao DM, Woosley JT. MRI of carcinoid tumors: spectrum of appearances in the gastrointestinal tract and liver. *J Magn Reson Imaging* 2001;14:261-9.
 23. Rockall AG, Planche K, Power N, Nowosinska E, Monson JP, Grossman AB, et al. Detection of neuroendocrine liver metastases with MnDPDP-enhanced MRI. *Neuroendocrinology* 2009;89:288-95.
 24. Owen NJ, Sohaib SA, Peppercorn PD, et al. MRI of pancreatic neuroendocrine tumours. *Br J Radiol* 2001;74(886):968-973.
 25. Sahani DV, Bonaffini PA, Fernandez-Del Castillo C, et al: Gastroenteropancreatic neuroendocrine tumors: role of imaging in diagnosis and management. *Radiology* 2013;266:38-61.
 26. De Angelis C, Carucci P, Repici A, Rizzetto M. Endosonography in decision-making and management of gastrointestinal endocrine tumors. *Eur J Ultrasound* 1999;10:139-50.
 27. Ishikawa T, Itoh A, Kawashima H, Ohno E, Matsubara H, Itoh Y, et al. Usefulness of EUS combined with contrast enhancement in the differential diagnosis of malignant versus benign and preoperative localization of pancreatic endocrine tumors. *Gastrointest Endosc* 2010;71:951-9.
 28. Khashab MA, Yong E, Lennon AM, Shin EJ, Amateau S, Hruban RH, et al. EUS is still superior to multidetector computerized tomography for detection of pancreatic neuroendocrine tumors. *Gastrointest Endosc* 2011;73:691-6.

29. Versari A, Camellini L, Carlinfante G, Frasoldati A, Nicoli F, Grassi E, et al. Ga-68 DOTATOC PET, endoscopic ultrasonography, and multidetector CT in the diagnosis of duodenopancreatic neuroendocrine tumors: a single-centre retrospective study. *Clin Nucl Med* 2010;35:321–8.
30. Atiq M, Bhutani MS, Bektas M, Lee JE, Gong Y, Tamm EP, et al. EUS-FNA for pancreatic neuroendocrine tumors: a tertiary cancer center experience. *Dig Dis Sci* 2012;57:791–800.
31. Cimitan M, Buonadonna A, Cannizzaro R, et al. Somatostatin receptor scintigraphy versus chromogranin A assay in the management of patients with neuroendocrine tumors of different types: clinical role. *Ann Oncol* 2003;14(7):1135–1141.
32. Kayani I, Bomanji JB, Groves A, et al. Functional imaging of neuroendocrine tumors with combined PET/CT using 68Ga-DOTATATE (DOTA-DPhe1,Tyr3-octreotate) and 18F-FDG. *Cancer* 2008;112(11):2447–2455.
33. Miederer M, Weber MM, Fottner C. Molecular imaging of gastroenteropancreatic neuroendocrine tumors. *Gastroenterol Clin North Am* 2010;39(4):923–935.
34. Oberg K. Diagnostic pathways. In: *Handbook of neuroendocrine tumors*. Bristol, England: BioScientifica, 2006; 101–121.
35. Taniyama Y, Suzuki T, Mikami Y, Moriya T, Satomi S, Sasano H. Systemic distribution of somatostatin receptor subtypes in human: an immunohistochemical study. *Endocr J* 2005;52(5):605–611.
36. Bakker WH, Krenning EP, Reubi JC, et al. In vivo application of [111In-DTPA-DPhe1]-octreotide for detection of somatostatin receptor-positive tumors in rats. *Life Sci* 1991;49(22):1593–1601.
37. Gibril F, Jensen RT. Diagnostic uses of radiolabelled somatostatin receptor analogues in gastroenteropancreatic endocrine tumours. *Dig Liver Dis* 2004;36:S106–20.
38. Lubberink M, Tolmachev V, Widström C, et al. 110mIn-DTPA-D-Phe1-octreotide for imaging of neuroendocrine tumors with PET. *J Nucl Med* 2002;43:1391–7.
39. Gabriel M, Decristoforo C, Kendler D, et al. 68Ga-DOTA-Tyr3-octreotide PET in neuroendocrine tumors: comparison with somatostatin receptor scintigraphy and CT. *J Nucl Med* 2007;48:508–18.
40. Buchmann I, Henze M, Engelbrecht S, et al. Comparison of 68Ga-DOTATOC PET and 111In-DTPAOC (Octreoscan) SPECT in patients with neuroendocrine tumours. *Eur J Nucl Med Mol Imaging* 2007;34:1617–26.
41. Geijer H, Breimer LH. Somatostatin receptor PET/CT in neuroendocrine tumours: update on systematic review and meta-analysis. *Eur J Nucl Med Mol Imaging* 2013;40:1770–80.
42. Sadowski SM, Neychev V, Millo C, et al. Prospective study of 68Ga-DOTATATE positron emission tomography/computed tomography for detecting gastroentero-pancreatic neuroendocrine tumors and unknown primary sites. *J Clin Oncol* 2016;34:588–96.
43. Hruban RH, Klimstra DS, Pitman MB. Tumors of the pancreas. In: *Atlas of tumor pathology*. Washington, DC: Armed Forces Institute of Pathology, 2007; 23–376.
44. Anderson MA, Carpenter S, Thompson NW, Nostrant TT, Elta GH, Scheiman JM. Endoscopic ultrasound is highly accurate and directs management in patients with neuroendocrine tumors of the pancreas. *Am J Gastroenterol* 2000;95:2271–7.
45. Plöckinger U, Rindi G, Arnold R, et al. Guidelines for the diagnosis and treatment of neuroendocrine gastrointestinal tumours. A consensus statement on behalf of the European Neuroendocrine Tumour Society (ENETS). *Neuroendocrinology* 2004;80(6):394–424.
46. Lewis RB, Lattin GE Jr, Paal E. Pancreatic endocrine tumors: radiologic-clinicopathologic correlation. *RadioGraphics* 2010;30(6):1445–1464.
47. Low G, Panu A, Millo N, Leen E. Multimodality imaging of neoplastic and nonneoplastic solid lesions of the pancreas. *RadioGraphics* 2011;31(4):993–1015.
48. Bordeianou L, Vagefi PA, Sahani D, et al. Cystic pancreatic endocrine neoplasms: a distinct tumor type? *J Am Coll Surg* 2008;206(3):1154–1158.

49. Heller MT, Shah AB. Imaging of neuroendocrine tumors. *Radiol Clin North Am* 2011;49(3):529–548.
50. Thoeni RF, Mueller-Lisse UG, Chan R, Do NK, Shyn PB. Detection of small, functional islet cell tumors in the pancreas: selection of MR imaging sequences for optimal sensitivity. *Radiology* 2000;214(2):483–490.
51. Alsohaibani F, Bigam D, Kneteman N, Shapiro AM, Sandha GS. The impact of preoperative endoscopic ultrasound on the surgical management of pancreatic neuroendocrine tumours. *Can J Gastroenterol* 2008;22(10):817–820.
52. Anaye A, Mathieu A, Closset J, Bali MA, Metens T, Matos C. Successful preoperative localization of a small pancreatic insulinoma by diffusion-weighted MRI. *JOP* 2009;10(5):528–531.
53. Wang Y, Chen ZE, Yaghmai V, et al. Diffusion-weighted MR imaging in pancreatic endocrine tumors correlated with histopathologic characteristics. *J Magn Reson Imaging* 2011;33(5):1071–1079.
54. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. *Cancer* 2003;97(4):934–959.
55. Levy AD, Sobin LH. From the archives of the AFIP: Gastrointestinal carcinoids: imaging features with clinicopathologic comparison. *RadioGraphics* 2007;27(1):237–257.
56. Bordi C. Gastric carcinoids. *Ital J Gastro- enterol Hepatol* 1999;31(Suppl 2):S94– S97.
57. Chang S, Choi D, Lee SJ, et al. Neuro- endocrine neoplasms of the gastrointestinal tract: classification, pathologic basis, and imaging features. *RadioGraphics* 2007;27(6):1667–1679.
58. Scherübl H, Jensen RT, Cadiot G, Stölzel U, Klöppel G. Neuroendocrine tumors of the small bowels are on the rise: Early as- pects and management. *World J Gastroin- test Endosc* 2010;2(10):325–334.
59. Pantongrag-Brown L, Buetow PC, Carr NJ, Lichtenstein JE, Buck JL. Calcification and fibrosis in mesenteric carcinoid tumor: CT findings and pathologic correlation. *AJR Am J Roentgenol* 1995;164:387–91.
60. Shapiro R, Eldar S, Sadot E, Papa MZ, Zip- pel DB. Appendiceal carcinoid at a large tertiary center: pathologic findings and long-term follow-up evaluation. *Am J Surg* 2011;201(6):805–808.
61. Anthony LB, Strosberg JR, Klimstra DS, et al. The NANETS consensus guidelines for the diagnosis and management of gastrointestinal neuroendocrine tumors (nets): well-differentiated nets of the distal colon and rectum. *Pancreas* 2010;39(6):767–774.
62. Prasad V, Ambrosini V, Hommann M, Hoersch D, Fanti S, Baum RP. Detection of unknown primary neuroendocrine tumours (CUP-NET) using (68)Ga-DOTA-NOC receptor PET/CT. *Eur J Nucl Med Mol Imaging* 2010;37(1):67–77.
63. Hauso O, Gustafsson BI, Kidd M, et al. Neuroendocrine tumor epidemiology: contrasting Norway and North America. *Can- cer* 2008;113(10):2655–2664.
64. Johanssen S, Boivin M, Lochs H, Voderholzer W. The yield of wireless capsule endoscopy in the detection of neuroendocrine tumors in comparison with CT enteroclysis. *Gastrointest Endosc* 2006;63(4):660–665.
65. Wang SC, Parekh JR, Zuraek MB, et al. Identification of unknown primary tumors in patients with neuroendocrine liver me- tastases. *Arch Surg* 2010;145(3):276–280.
66. Sommer WH, Zech CJ, Bamberg F, Auernhammer CJ, Helck A, Paprottka PM, et al. Fluid-fluid level in hepatic metastases: a characteristic sign of metastases of neuroendocrine origin. *Eur J Radiol* 2012;81:2127–32.
67. Elias D, Lefevre JH, Duvillard P, et al. Hepatic metastases from neuroendocrine tumors with a “thin slice” pathological examination: they are many more than you think. *Ann Surg* 2010;251(2):307–310.
68. Gibril F, Jensen RT. Diagnostic uses of radiolabelled somatostatin receptor analogues in gastro- enteropancreatic endocrine tumours. *Dig Liver Dis* 2004;36(Suppl 1):S106–S120.
69. Modlin IM, Oberg K, Chung DC, et al. Gastroenteropancreatic neuroendocrine tumours. *Lancet Oncol* 2008;9(1):61–72.

70. Kulke MH, Anthony LB, Bushnell DL, et al. NANETS treatment guidelines: well- differentiated neuroendocrine tumors of the stomach and pancreas. *Pancreas* 2010;39(6):735–752.
71. Arnold R, Chen YJ, Costa F, et al. ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: follow-up and documentation. *Neuroendocrinology* 2009;90(2):227–233.
72. Oberg K, Knigge U, Kwekkeboom D, ESMO Guidelines Working Group et al (2012) Neuroendocrine gastro-entero-pancreatic tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 23(Suppl 7):vii124–vii130
73. Pavel M, Baudin E, Couvelard A et al (2012) ENETS Consensus Guidelines for the management of patients with liver and other distant metastases from neuroendocrine neoplasms of foregut, midgut, hindgut, and unknown primary. *Neuroendocrinology* 95:157–176
74. Peppia M, Brountzos E, Economopoulos N et al (2009) Embolization as an alternative treatment of insulinoma in a patient with multiple endocrine neoplasia type 1 syndrome. *Cardiovasc Intervent Radiol* 32:807–811
75. Moore T, Peterson L, Harington D (1982) Successful arterial embolization of an insulinoma. *JAMA* 248:1953–1955
76. Uflacker R (1992) Arterial embolization as definitive treatment for benign insulinoma of the pancreas. *J Vasc Interv Radiol* 3:441–639 discussion 644–666
77. Rott G, Biggemann M, Pfohl M (2008) Embolization of an insulinoma of the pancreas with trisacryl gelatin microspheres as definitive treatment. *Cardiovasc Intervent Radiol* 31:659–662
78. Ben-Ishay O, Linder R, Ofer A et al (2012) Hypervascular lesion in the head of the pancreas. Preoperative angiography and selective embolization results in bloodless operation. *JOP* 13:671–673
79. Rossi M, Orgera G, Hatzidakis A et al (2014) Minimally invasive ablation treatment for locally advanced pancreatic adenocarcinoma. *Cardiovasc Intervent Radiol* 37:203–210
80. Goldberg SN, Mallery S, Gazelle GS et al (1999) EUS-guided radiofrequency ablation in the pancreas: results in a porcine model. *Gastrointest Endosc* 50:392–401
81. Matsui Y, Nakagawa A, Kamiyama Y et al (2000) Selective thermocoagulation of unresectable pancreatic cancers by using radiofrequency capacitive heating. *Pancreas* 20:14–20
82. Limmer S, Huppertb P, Juettea V et al (2009) Radiofrequency ablation of solitary pancreatic insulinoma in a patient with episodes of severe hypoglycemia. *Eur J Gastroenterol Hepatol* 21:1097–1101
83. Akhlaghpour S, Dahi F, Alinaghizadeh M et al (2011) CT fluoroscopy-guided transcaval radiofrequency ablation of insulinoma. *J Vasc Interv Radiol* 22:409–410
84. Gupta S, Johnson MM, Murthy R et al (2005) Hepatic arterial embolization and chemoembolization for the treatment of patients with metastatic neuroendocrine tumors: variables affecting response rates and survival. *Cancer* 104:1590–1602
85. Strosberg JR, Choi J, Cantor AB et al (2006) Selective hepatic artery embolization for treatment of patients with metastatic carcinoid and pancreatic endocrine tumors. *Cancer Control* 13:72–78
86. Sofocleous CT, Petre EN, Gonen M et al (2013) Factors affecting periprocedural morbidity and mortality and long-term patient survival after arterial embolization of hepatic neuroendocrine metastases. *J Vasc Interv Radiol* 25:22–30
87. Kress O, Wagner HJ, Wied M et al (2003) Transarterial chemoembolization of advanced liver metastases of neuroendocrine tumors—a retrospective single-center analysis. *Digestion* 68:94–101
88. Ruutiainen AT, Soulen MC, Tuite CM et al (2007) Chemoembolization and bland embolization of neuroendocrine tumor metastases to the liver. *J Vasc Interv Radiol* 18:847–855
89. Bhagat N, Reyes DK, Lin M et al (2013) Phase II study of chemoembolization with drug-eluting beads in patients with hepatic neuroendocrine metastases: high incidence of biliary injury. *Cardiovasc Intervent Radiol* 36:449–459

90. King J, Quinn R, Glenn DM et al (2008) Radioembolization with selective internal radiation microspheres for neuroendocrine liver metastases. *Cancer* 113:921–929
91. Rhee TK, Lewandowski RJ, Liu DM et al (2008) 90Y radio- embolization for metastatic neuro- endocrine liver tumors: pre- liminary results from a multi-institutional experience. *Ann Surg* 247:1029–1035
92. Kennedy AS, Dezarn WA, McNeillie P et al (2008) Radioembolization for unresectable neuro- endocrine hepatic metastases using resin 90Y-microspheres: early results in 148 patients. *Am J Clin Oncol* 31:271–279
93. Akyildiz HY, Mitchell J, Milas M et al (2010) Laparoscopic radiofrequency thermal ablation of neuroendocrine hepatic metastases: long-term follow-up. *Surgery* 148:1288–1293
94. Mazzaglia PJ, Berber E, Milas M et al (2007) Laparoscopic radiofrequency ablation of neuro- endocrine liver metastases: a 10-year experience evaluating predictors of survival. *Surgery* 142:10–19