ESMO ADVANCED COURSE ON

Individualising the therapeutic approach in patients with NENs

Terminology, diagnosis, characterisation and staging

Role of Radiology

Guido Bonomo
Friday, 14 June 2019
DISCLOSURES

- Pfizer Europe, fee and travel expenses
ROLE OF RADIOLOGY

History

Computed tomography of malignant carcinoid disease.
McCarty SB, Stark CD, Vasan AA, Goldsteen I.
Abstract
Twenty-two patients with malignant carcinoid syndrome were evaluated with CT, the largest series to date. A mass representing the primary tumor or local adenopathy was identified in four patients, appearing as a homogeneous mass involving mesentry and bowel. In two other patients the primary was not identifiable by barium series, angiography, CT, or laparotomy. In the remaining 16 patients who were scanned after resection of the primary tumor had mesenteric thickening and free fluid. Malignant ascites was present in seven of 21 patients. All hepatic metastases were hypodense on the precontrast study. The effect of contrast administration on lesion detectability was variable, obscuring at least one or more metastases in eight of 21 scans. We recommend noncontrast scans of the liver in patients in whom the number and size of metastases are critical to therapy.

PMID: 94221

Computed tomography and angiography in carcinoid liver metastases.
Steck B, Watanapiro F, Ashby T.
Abstract
Fifteen patients with carcinoid metastases in the liver were examined with computed tomography (CT). In 13 patients, liver metastases were demonstrated, while 2 patients had a normal liver at CT. The attenuation of the metastases was lower than that of the liver parenchyma in 12 patients, higher in one. Angiography was performed on 10 patients, and liver metastases were diagnosed in 9. Eight patients had hypervascular metastases with dense accumulation of contrast medium. In one patient, displacement of the intrahepatic arteries was the only sign of an expansive process. In one patient, previously treated with Iodine of the common hepatic artery, no signs of liver metastases could be revealed at angiography, but were evident at CT.

PMID: 3529271

Computed Tomography of Abdominal Carcinoid Tumors

Computed tomography (CT) scans were obtained in 20 patients with primary or metastatic abdominal carcinoid tumors. The primary tumors were seen rarely on CT. Mesenteric involvement was seen in eight of the 20 patients, usually as a soft-tissue mass surrounded by fat and radiating soft-tissue strands. Enlarged retroperitoneal lymph nodes were seen in seven patients, but rarely were they the only manifestation of intraabdominal disease. The most common finding was liver metastases (13 of 20 patients). CT is helpful in evaluating the extent of tumor before surgical exploration and in following the progression of disease once the diagnosis has been established.

AJR 143:581-584, September 1984
0361-8033/84/1433-0581
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Gastroenteropancreatic Neuroendocrine Tumors: Role of Imaging in Diagnosis and Management¹

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are a heterogeneous group of neoplasms that arise from cells of the diffuse neuroendocrine system and are characterized by a wide spectrum of clinical manifestations. All NETs are potentially malignant but differ in their biologic characteristics and the probability of metastatic disease. The pathologic classification of these tumors relies on their proliferation and differentiation. In the past decades, several nomenclatures have been proposed to stratify neuroendocrine tumors, but the World Health Organization classification is the one that is most widely accepted and used. The diagnosis of neuroendocrine tumor relies on clinical manifestation, laboratory parameters, imaging features, and tissue biomarkers in a biopsy specimen. With improved understanding of the natural history and lesion biology, management of GEP-NETs has also evolved. Although surgery remains the only potentially curative therapy for patients with primary GEP-NETs, other available treatments include chemotherapy, interferon, somatostatin analogs, and targeted therapies. Recent improvements in both morphologic and functional imaging methods have contributed immensely to patient care. Morphologic imaging with contrast agent–enhanced multidetector computed tomography and magnetic resonance imaging is most widely used for initial evaluation and staging of disease in these patients, whereas functional imaging techniques are useful both for detection and prognostic evaluation and can change treatment planning.
ROLE OF RADIOLOGY

Background

Table 5

<table>
<thead>
<tr>
<th>Site</th>
<th>Multidetector CT</th>
<th>MR Imaging</th>
<th>SRF</th>
<th>FDG PET</th>
<th>Endoscopic US or Endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional</td>
<td>Small (&lt; 2 cm), well-defined, hyperintense.</td>
<td>Additional features: T2 hyperintensities, T1 hypointensity.</td>
<td>Best modality for small tumor detection (67).</td>
<td>Insulinomas: 14–52% sensitivity, 100% specificity.</td>
<td></td>
</tr>
<tr>
<td>Nonfunctional</td>
<td>Large (&gt; 4 cm) capsule, heterogeneous enhancement, necrotic or cystic changes are common, occasionally purely hypointense, calcifications in malignant tumors, local invasion and metastases (up to 80% of cases) (6).</td>
<td>Additional features: T2 hyperintensities, T1 hypointensity. Problem solving.</td>
<td>Tissue diagnosis in incidental lesions.</td>
<td>Insulinomas: 14–52% sensitivity, 100% specificity.</td>
<td></td>
</tr>
<tr>
<td>Performance (%)</td>
<td>74–94 (43,89,81)</td>
<td>74–94 (43,89,81)</td>
<td>84.2–91.7 (67).</td>
<td>84.2–91.7 (67).</td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>Stomach</td>
<td>Types I and II are enhancing polyloid or submucosal lesions &lt; 2 cm; larger lesions may have ulceration; CT might miss lesions &lt; 1 cm; CT and double-contrast barium studies yield findings similar to those of other submucosal or polyloid lesions; type II are large (1–2 cm) with infiltrative morphology (malignant) and may be indistinguishable.</td>
<td>Gas troscopy to look for lesion, findings similar to those of other submucosal or polyloid lesions; endoscopic US for evaluation of depth of tumor invasion in wall and biopsy.</td>
<td>Gas troscopy to look for lesion, findings similar to those of other submucosal or polyloid lesions; endoscopic US for evaluation of depth of tumor invasion in wall and biopsy.</td>
<td></td>
</tr>
</tbody>
</table>

Table 5 (continued)

<table>
<thead>
<tr>
<th>Site</th>
<th>Multidetector CT</th>
<th>MR Imaging</th>
<th>SRF</th>
<th>FDG PET</th>
<th>Endoscopic US or Endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small bowel</td>
<td>Hypervascular lesion (intraperitoneal or mesenteric), bowel thickening; additional findings: desmoplastic reaction (mesenteric, mesoenteric) insulinomas with or without calcification; calcification in 70% of mesenteric nodal metastases; complications: bowel obstruction, loss of function; infection; sensitivity of CT enterography: 90%–95% (68).</td>
<td>Additional features: T2 hyperintensities, T1 hypointensity; test evoked by oral or parenteral contrast.</td>
<td>Test evoked by oral or parenteral contrast.</td>
<td>Test evoked by oral or parenteral contrast.</td>
<td></td>
</tr>
<tr>
<td>Appendix</td>
<td>Generally small (&lt; 2 cm) enhancing lesions; diffuse circumferential mural thickening; possible associated findings of appendicitis (primary tumor may not be readily seen).</td>
<td>Insulinomas: 14–52% sensitivity, 100% specificity.</td>
<td>84.2–91.7 (67).</td>
<td>84.2–91.7 (67).</td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td>Generally small (&lt; 2 cm) scirrhous lesions more common in ascending (right) colon; rectosigmoid; rectal obstruction.</td>
<td>Insulinomas: 14–52% sensitivity, 100% specificity.</td>
<td>84.2–91.7 (67).</td>
<td>84.2–91.7 (67).</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>Generally small (&lt; 2 cm) submucosal lesions. Endoscopic small polyps or polyloid mass; endoscopic US for evaluation of depth of tumor invasion in wall and biopsy.</td>
<td>Insulinomas: 14–52% sensitivity, 100% specificity.</td>
<td>84.2–91.7 (67).</td>
<td>84.2–91.7 (67).</td>
<td></td>
</tr>
<tr>
<td>Metastases</td>
<td>Same as for pancreas.</td>
<td>Insulinomas: 14–52% sensitivity, 100% specificity.</td>
<td>84.2–91.7 (67).</td>
<td>84.2–91.7 (67).</td>
<td></td>
</tr>
<tr>
<td>Note: --- Numbers in parentheses are references.</td>
<td>Insulinomas: 14–52% sensitivity, 100% specificity.</td>
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<td>Insulinomas: 14–52% sensitivity, 100% specificity.</td>
<td></td>
</tr>
</tbody>
</table>
1. Advantages include faster acquisition, improved spatial resolution, and multiplanar display.  
2. Advantages include increased detection of early-stage disease and ability to detect and characterize small lesions in pancreas and liver.  
3. Advantages include utility for lesions expressing SST2 and ability to evaluate patients for bariatric therapies.  
4. Advantages include ability to demonstrate malignant and poorly differentiated tumors.  
5. Advantages include ability to demonstrate small lesions and to guide biopsy.

ESMO
ROLE OF RADIOLOGY

Background

- Imaging
- staging
- monitoring
- Treatment planning
ROLE OF RADIOLOGY
Ileal NETs

- Primary ileal NETs originate in the submucosal layer from enterochromaffin cells and can be solitary or multifocal.
- Their slow growth and initial vague nonspecific symptoms can lead to a long delay in diagnosis.
- Patients are typically between 50 and 70 yrs old, often with vague intermittent abdominal pain.
- Syndrome (flushing, sweating, watery diarrhea) only occurs in 10% of patients, after the development of metastatic disease.
ROLE OF RADIOLOGY

Ileal NETs- CT

- Primary tumor can be difficult to detect because of its small size
- Routine CT offers sensitivity as low as 60% in identifying a primary small bowel NET
- Visible tumors manifest as submucosal plaquelike or polypoid masses or nodular areas of wall thickening
ROLE OF RADIOLOGY
Ileal NENs- CT

- Mesenteric disease is often present at time of diagnosis.
- Small primary tumors are at high risk for mesenteric metastasis, with almost 50% of tumors <1 cm and 22% of tumors <0.5 cm presenting with nodal disease.
- The likelihood of liver involvement is related to the size of the primary tumor: 20-30% in tumors <1 cm, 40% in tumors >2 cm.
ROLE OF RADIOLOGY

Ileal NETs- CT

CT-Enterography May Identify Small Bowel Tumors Not Detected by Capsule Endoscopy: Eight Years Experience at Mayo Clinic Rochester

Fayaz A. Hakim · Jeffrey A. Alexander · James E. Huprich · Madhusudan Grover · Felicity T. Enders

CT-Enterography

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTE</td>
<td>92.7% (80.1–98.5)</td>
</tr>
<tr>
<td>CE</td>
<td>29.6% (13.8–50.2)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
</tbody>
</table>

CT-Enterography provides improved tumor-to-background contrast resolution by utilizing neutral oral contrast medium, with sensitivity for detecting small bowel tumors approaching 93%.
Pancreatic NETs are a heterogeneous group of tumors that arise from neuroendocrine cells of the pancreas.

PanNETs account for 2% of all pancreatic neoplasms and have an incidence of 1-2 per 100,000 per year.

Clinically are divided into hyperfunctioning (functional) or non-hyperfunctioning (non-functional), depending on the presence of a specific clinical syndrome, caused by hormonal hypersecretion.
ROLE OF RADIOLOGY
Pancreatic NETs- CT

Contrast enhanced CT and/or MRI are the initial imaging techniques for patients with suspected pancreatic tumor. Typically present as small, well-demarcated, homogeneously enhanced hypervascular lesions. Yet up to 41% are hypovascular. Tumor hypovascularity is due to lower microvessel count, extensive fibrosis, or the presence of necrosis, calcifications (less differentiated PanNETs G2-G3).
The role of multimodal imaging in guiding resectability and cytoreduction in pancreatic neuroendocrine tumors: focus on PET and MRI

Laura Rozenblum1,2 · Fatima-Zohra Mokrane2,3 · Randy Yeh4 · Mathieu Sinigaglia5 · Florent Besson6 · Romain-David Seban7 · Cecile N Chougnet8 · Paul Revel-Mouroz9 · Binsheng Zhao3 · Philippe Otal7 · Lawrence H. Schwartz3 · Laurent Dercle3,9

Abstract
Pancreatic neuroendocrine tumors (pNETs) are rare neoplasms that secrete peptides and neuro-amines. pNETs can be sporadic or hereditary, syndromic or non-syndromic with different clinical presentations and prognoses. The role of medical imaging includes locating the tumor, assessing its extent, and evaluating the feasibility of curative surgery or cytoreduction. Pancreatic NETs have very distinctive phenotypes on CT, MRI, and PET. PET have been demonstrated to be very sensitive to detect either well-differentiated pNETs using 68Ga-labeled somatostatin receptor (SSTR) radiotracers, or more aggressive undifferentiated pNETs using 18F-FDG. A comprehensive interpretation of multimodal imaging guides resectability and cytoreduction in pNETs. The imaging phenotype provides information on the differentiation and proliferation of pNETs, as well as the spatial and temporal heterogeneity of tumors with prognostic and therapeutic implications. This review provides a structured approach for standardized reading and reporting of medical imaging studies with a focus on PET and MR techniques. It explains which imaging approach should be used for different subtypes of pNET and what a radiologist should be looking for and reporting when interpreting these studies.
ROLE OF RADIOLOGY
Pancreatic NETs imaging

F 47 y.o. PanNET G2, Ki 67 10%, well diff, liver mets

Multidisciplinary meeting: In consideration of the biology of the disease, clinical history and good clinical conditions, hepatic locoregional treatment is proposed with hepatic embolization after re-evaluation morphology with chest CT abdomen pelvis with contrast agent + PET / CT Ga68 and subsequent possible surgery on site of the primary tumor.
ROLE OF RADIOLOGY
Pancreatic NETs imaging

PET/CT Ga68
ROLE OF RADIOLOGY
Pancreatic NETs imaging

Superselective bland embolization

Angiography

Surgery
ROLE OF RADIOLOGY
GEP-NETs liver metastases

Pattern and risk factors for distant metastases in gastrointestinal neuroendocrine neoplasms: a population-based study
Wen Cai, Yinuo Tan, Weiling Ge, Kefeng Ding & Hanguang
Cancer Medicine 2018; 7(6):2699–2709

Figure 4. Metastasis pattern of NECs and NETs separated by primary site.
ROLE OF RADIOLOGY

GEP-NETs liver metastases

- The liver has a double blood supply from hepatic artery and portal vein, with a ratio of 1:4
ROLE OF RADIOLOGY

GEP-NETs liver metastases

All liver tumors are fed by the hepatic artery

THE BLOOD SUPPLY OF NEOPLASMS IN THE LIVER

Charles Breed, M.D., and Gang Young, M.D.
(From the Department of Pathology, University of Pennsylvania School of Medicine, Philadelphia, Pa., and the Pathology Research Institute, Medical College, National Sun Yat Sen University, Canton, China)


SUMMARY AND CONCLUSIONS

By means of injection experiments it was shown that malignant neoplasms growing in the liver tend to acquire an exclusively arterial blood supply.

### Table II

<table>
<thead>
<tr>
<th>Primary tumor</th>
<th>Approximate number of metastases examined</th>
<th>Size of metastases</th>
<th>Blood supply of tumors*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma, breast</td>
<td>300</td>
<td>10–30</td>
<td>% 80</td>
</tr>
<tr>
<td>Undifferentiated carcinoma, breast</td>
<td>50</td>
<td>1–10</td>
<td>% 95</td>
</tr>
<tr>
<td>Adenocarcinoma, bronchus</td>
<td>200</td>
<td>2–35</td>
<td>% 100</td>
</tr>
<tr>
<td>Adenocarcinoma, bronchus</td>
<td>500</td>
<td>2–50</td>
<td>% 100</td>
</tr>
<tr>
<td>Undifferentiated carcinoma, kidney</td>
<td>200</td>
<td>3–35</td>
<td>% 95</td>
</tr>
<tr>
<td>Squamous cell carcinoma, cervix</td>
<td>10</td>
<td>20–50</td>
<td>% 100</td>
</tr>
<tr>
<td>Adenocarcinoma, sigmoid</td>
<td>10</td>
<td>0.5–1</td>
<td>% 80</td>
</tr>
<tr>
<td>Adenocarcinoma, sigmoid</td>
<td>10</td>
<td>1–3</td>
<td>% 100</td>
</tr>
<tr>
<td>Adenocarcinoma, stomach</td>
<td>50</td>
<td>2–100</td>
<td>% 100</td>
</tr>
<tr>
<td>Adenocarcinoma, rectum</td>
<td>2</td>
<td>15 and 30</td>
<td>% 95</td>
</tr>
<tr>
<td>Adenocarcinoma, colon</td>
<td>1</td>
<td>7</td>
<td>% 100</td>
</tr>
</tbody>
</table>

* The blood supply was estimated by determining the number of vessels per low-power field that were filled by the respective arterial and portal injection masses.
ROLE OF RADIOLOGY
GEP-NETs liver metastases

Liver met from unknown origin NET

CT-portal phase
CT-common hepatic artery injection of cm
CT-left lobe artery injection of cm
CT-lesion feeder arteries injection of cm
ROLE OF RADIOLOGY
GEP-NETs liver metastases

Hypervascular Liver Lesions
Aya Kamaya, MD, Katherine E. Maturen, MD,† Grace A. Tye, MD,‡ Yueyi I. Liu, MD, PhD,‡ Naveen N. Parti, MD,§ and Terry S. Desser, MD*


CT and MR sequential scan:
early arterial phase (20")
late arterial phase (35")
portal phase (70")
venous phase (150")

Enhancement Technique
Several studies have examined the timing of the contrast bolus in computed tomography (CT) and magnetic resonance imaging (MRI) for optimal conspicuity of hypervascular lesions.²⁻⁵
Most studies agree that late arterial-phase images of the liver provide the best lesion visibility. Late arterial enhancement of the liver is defined as the state of liver enhancement corresponding to early portal venous filling, slight parenchymal enhancement, and no hepatic venous enhancement. Timing of the late arterial phase is generally accepted as 9-16 seconds after enhancement of the abdominal aorta,²,⁶ or approximately 35 seconds after the antecubital injection of intravenous contrast.⁵
ROLE OF RADIOLOGY
GEP-NETs liver metastases

- Conspicuity of hepatic lesions on diagnostic imaging studies depends on adequate contrast with the normal liver parenchyma.
- The intratumoral vascular pattern (vessel size, density, a/v shunt) can influence the flow resistance and consequently the speed of the flow directed to the tumor.
- Contrastographic enhancement is closely related to the intratumoral vascular pattern.
Role of Radiology
Pancreatic NETs imaging

F 51 y.o. PanNET G1, Ki 67 3%, well diff, liver mets

Treatments: Dec ’17 CT diagnosis pancreatic mass + liver mets. Biopsy: PanNET G1, Ki 67 <3%. Jan ’18 PET Ga68: positive SSR on both primary and mets. Starts SSA Feb-Dec ’18 Sunitinib → TAE
Liver metastases of neuroendocrine tumors: is it possible to diagnose different histologic subtypes depending on multiphasic CT features?

Basak Gulpinar¹ · Elif Peker¹ · Melahat Kul¹ · Atilla Halil Elhan² · Nuray Haliloglu¹

Many studies in the literature have investigated the role of computerized tomography in the evaluation of NETs while a few of them have examined multiphasic CT features of the neuroendocrine tumor liver metastases [8–11]. Most of these studies have shown that most NET liver metastases are hyperattenuating on arterial phase and hypoattenuating on portal venous images; therefore, a dual phase CT is more reliable than a single phase CT in identifying arterial phase hyperenhancement liver metastases [8–11]. Most of these studies regarded the enhancement pattern of all NETs as similar regardless of the primary tumor’s origin [2]. Differentiation of histologic subtypes has not been extensively studied.
ROLE OF RADIOLOGY
GEP-NETs liver metastases

- NET liver mets often may be “hypervascular”....

Well differentiated duodenal NET
ROLE OF RADIOLOGY
GEP-NETs liver metastases

...sometimes they may be “hypovascular”
ROLE OF RADIOLOGY

GEP-NETs liver metastases

- Take care of pitfalls risk

Poor differentiated unknown origin NET

20°

70°
ROLE OF RADIOLOGY

GEP-NETs liver metastases

F 49 y.o. PanNET G2 Ki67 5%, med grade, non functioning. 2010 Surgery on primary site: staging acc. ENETS IIIb, pT2, pN1, G2, R0.
6/2014 multiple liver resections. 10/2014 PET/CT Ga68 multiple liver mets.
6/2015 → 9/2015 Everolimus + BYL719 (alpelisib)- STOP liver PD at CT
Detection of Liver Metastases From Endocrine Tumors: A Prospective Comparison of Somatostatin Receptor Scintigraphy, Computed Tomography, and Magnetic Resonance Imaging
Clarisse Dronca, Thierry de Baere, Jean Lumbrous, Hubert Caillier, Agnès Laplanche, Valérie Boige, Michel Ducrucx, Pierre Duveillard, Dominique Elias, Martin Schlemmer, Robert Sijal, and Eric Baudin

In conclusion, MRI depicted by far the greatest number of hepatic metastases in patients with WDEGP ET\textsuperscript{R}. This imaging modality, therefore, appears to be the procedure of choice for initial staging and liver evaluation before surgery, embolization, or radiofrequency in patients with ET. The low performance of SRS was mainly explained by the effect of the size of liver metastases on its detection capacity.

Well-differentiated gastroenteropancreatic (WDEGP) neuroendocrine tumors (ET),
ROLE OF RADIOLOGY
GEP-NETs liver metastases

Liver specific T1-cm enhances particular liver mets

Well differentiated testis NET

T1 T2 T1 fs mdc T1 fs mdc T1 fs mdc
ROLE OF RADIOLOGY
GEP-NETs liver metastases

Right colon NET G2, Ki67 7%
Tumor growth rate (TGR) is an alternative imaging based calculation that provides quantitative information on the change in tumor size over time (% per month), based on data from two imaging scans.
ROLE OF RADIOLOGY

GEP-NETs liver metastases

Value of Tumor Growth Rate (TGR) as an Early Biomarker Predictor of Patients’ Outcome in Neuroendocrine Tumors (NET)—The GREPONET Study

Angela Lamarca,1,2,3 Joakim Crona,4 Maxime Ronot,1 Marta Opanieszka,5 Carlos Lopez Lopez,1 Daniela Pizzuti,6 Pawan Nairan,2 Livia Carvalho,7 Regis Ottaviani Franzo Bezerra,8,9 Philip Borg,8 Nair Vietti Violi,9 Hector Vidal Trujeque,1 Louis de Mestier,2 Nils L. Schaler,4 Anders Sundin,2 Frederico Costa,6 Marianne Pavesi,7 Clarisse Driess,9 on behalf of The Knowledge Network

The Oncologist 2019;24:1–9 www.TheOncologist.com

Abstract

Introduction. Tumor growth rate (TGR; percent size change per month [%/m]) is postulated to be an early radiological biomarker to overcome limitations of RECIST. This study aimed to assess the impact of TGR in neuroendocrine tumors (NETs) and potential clinical and therapeutic applications.

Materials and Methods. Patients (pts) with advanced grade (G) 1/2 NETs from the pancreas or small bowel initiating systemic treatment (ST) or watch and wait (WW) were eligible. Baseline and follow-up scans were retrospectively reviewed to calculate TGR at pretreatment (TGR0), first follow-up (TGR22), and 3 (±1) months of study entry (TGR3m).

Results. Out of 905 pts screened, 222 were eligible. Best TGR22 (222 pts) cutoff was 0.8 (area under the curve, 0.74). When applied to TGR22, 103 pts with TGR3m <0.8 (66.9%) versus TGR3m ≥0.8 (33.1%) had longer median progression-free survival (PFS; 26.3 m; 95% confidence interval [CI] 19.5–32.4 vs. 9.3 m; 95% CI, 6.1–22.9) and lower progression rate at 12 months (7.3% vs. 56.6%; p = .001). WW (vs. ST) and TGR3m ≥0.8 (hazard ratio [HR], 3.75; 95% CI, 2.21–6.34; p < .001) were retained as factors associated with shorter PFS in multivariable Cox regression. TGR22 (HR, 3.62; 95% CI, 1.97–6.64; p < .001) was also an independent factor related to shorter PFS when analysis was limited to pts with stable disease (81 pts). Out of the 60 pts with TGR22 data available, 60% of pts had TGR0 < 4%/month. TGR0 ≥4%/month (HR, 2.22; 95% CI, 1.15–4.31; p = .018) was also an independent factor related to shorter PFS.

Conclusion. TGR is an early radiological biomarker able to predict PFS and to identify patients with advanced NETs who may require closer radiological follow-up. The Oncologist 2019;24:1–9

Implications for Practice: Tumor growth rate at 3 months (TGR3m) is an early radiological biomarker able to predict progression-free survival and to identify patients with advanced neuroendocrine tumors who may require closer radiological follow-up. It is feasible to calculate TGR3m in clinical practice and it could be a useful tool for guiding patient management. This biomarker could also be implemented in future clinical trials to assess response to therapy.
ROLE OF RADIOLOGY

Conclusions

- Imaging plays a crucial role in both the diagnosis and management of GEP NETs patients
- The exams must be complete from a technical point of view in order to reduce the risk of errors with clinical consequences
- Multimodality imaging should be considered for clinical decision making
- Dedicated Radiologist should be constantly involved in the multidisciplinary meeting and sensitized on the problems of patients affected by GEP NETs