
به نام خدای مهربان

Radionuclide Therapy in Pediatric Oncology

Theragnostics (Theranostics) is a new field of medicine which combines specific targeted **therapy** based on specific targeted **diagnostic** tests.

Theragnostics provide a transition from conventional medicine to contemporary personalised and precision medicine approach.

The **theragnostics** paradigm involves using nanoscience to unite diagnostic and therapeutic applications to form a single agent, allowing for diagnosis, drug delivery and treatment response monitoring.

The traditional approach to managing pediatric patients with DTC included reflexive postsurgical **131I** therapy, which was prescribed in an effort to eliminate residual thyroid tissue in order to increase sensitivity for using serum Tg as a biomarker for recurrent disease.

In addition, **131I** was prescribed in an effort to decrease the risk of recurrent disease.

Therefore, the goal of **131I** therapy is to decrease the risks of thyroid cancer recurrence and theoretically to improve mortality by eliminating iodine-avid disease

TABLE 6. AMERICAN THYROID ASSOCIATION PEDIATRIC THYROID CANCER RISK LEVELS AND POSTOPERATIVE MANAGEMENT IN CHILDREN WITH PAPILLARY THYROID CARCINOMA

2015

ATA pediatric risk level[a]	*Definition*	*Initial postoperative staging*[b]	*TSH goal*[c]	*Surveillance of patients with no evidence of disease*[d]
Low	Disease grossly confined to the thyroid with N0/Nx disease or patients with incidental N1a disease (microscopic metastasis to a small number of central neck lymph nodes)	Tg[e]	0.5–1.0 mIU/L	US at 6 months postoperatively and then annually × 5 years Tg[e] on LT_4 every 3–6 months for 2 years and then annually
Intermediate	Extensive N1a or minimal N1b disease	TSH-stimulated Tg[e] and diagnostic ^{123}I scan in most patients (see Fig. 2)	0.1–0.5 mIU/L	US at 6 months postoperatively, every 6–12 months for 5 years, and then less frequently Tg[e] on LT_4 every 3–6 months for 3 years and then annually Consider TSH-stimulated Tg[e] ± diagnostic ^{123}I scan in 1–2 years in patients treated with ^{131}I
High	Regionally extensive disease (extensive N1b) or locally invasive disease (T4 tumors), with or without distant metastasis	TSH-stimulated Tg[e] and diagnostic ^{123}I scan in all patients (see Fig. 2)	<0.1 mIU/L	US at 6 months postoperatively, every 6–12 months for 5 years, and then less frequently Tg[e] on LT_4 every 3–6 months for 3 years and then annually TSH-stimulated Tg[e] ± diagnostic ^{123}I scan in 1–2 years in patients treated with ^{131}I

2022 ETA Guidelines for management of pediatric thyroid nodules and differentiated thyroid carcinoma.

131I therapy for benign and malignant thyroid disease has been successfully used for 80 years. Over this time, it has been applied extensively in adult and in pediatric patients alike and has contributed to a normalization of life expectancy in DTC.

In pediatric patients in particular, **131I** therapy can be extremely helpful, even in case of disseminated pulmonary metastases, patients may be cured by one or more courses of **131I**.

2022 ETA Guideline for management of pediatric thyroid nodules and differentiated thyroid carcinoma.

We suggest that 131I therapy is indicated for **all children** following total thyroidectomy, for the treatment of persistent locoregional disease, remnant thyroid cells, or nodal disease that cannot be resected and iodine avid distant metastases.

131I is indicated for treatment of nodal or other locoregional disease that is not amenable to surgery as well as distant metastases that are known or presumed to be iodine-avid.

In addition, some experts also advocate routine **131I** therapy for children with T3 tumors or extensive regional nodal involvement (extensive N1a or N1b disease).

Published studies show that children with iodine-avid pulmonary metastases benefit from **131I** treatment, and complete remission is achievable for many patients, particularly those with microscopic and small-volume lung disease.

The short-term side effects of **131I** are well known and include damage to tissues that incorporate iodine, resulting in sialadenitis, xerostomia, dental caries, ocular dryness, and nasolacrimal duct obstruction.

Strategies exist to help treat or prevent **131I**-related side effects; but none of these prophylactic measures have been formally studied in the pediatric population.

In postpubertal males, transient rise in FSH is common and may persist for up to 18 months after **131I** exposure.

Increasing cumulative activities of **131I** may lead to decreased spermatogenesis generally without an effect on testosterone production.

Current guidelines recommend that males avoid attempts at conception for at least 4 months post 131I therapy. Postpubertal testes appear to be more vulnerable than prepubertal testes to the toxic effects of ionizing radiation.

Therefore, postpubertal males should be counseled and sperm banking should be considered for those receiving cumulative activities ≥ 400 mCi.

Transient amenorrhea and menstrual irregularities are reported in up to 17% of females under age of 40 years.

This is true despite the fact that 65% of young women received a single low activity of **131I** (average = 81 mCi).

Collectively, these data have led to the recommendation that conception should be avoided during the year immediately following **131I** administration.

Transient BM suppression, Lung fibrosis and second primary cancer …
rH-TSH

There are clear **benefits** and **risks**, both acute and chronic, following administration of **131I** during childhood.

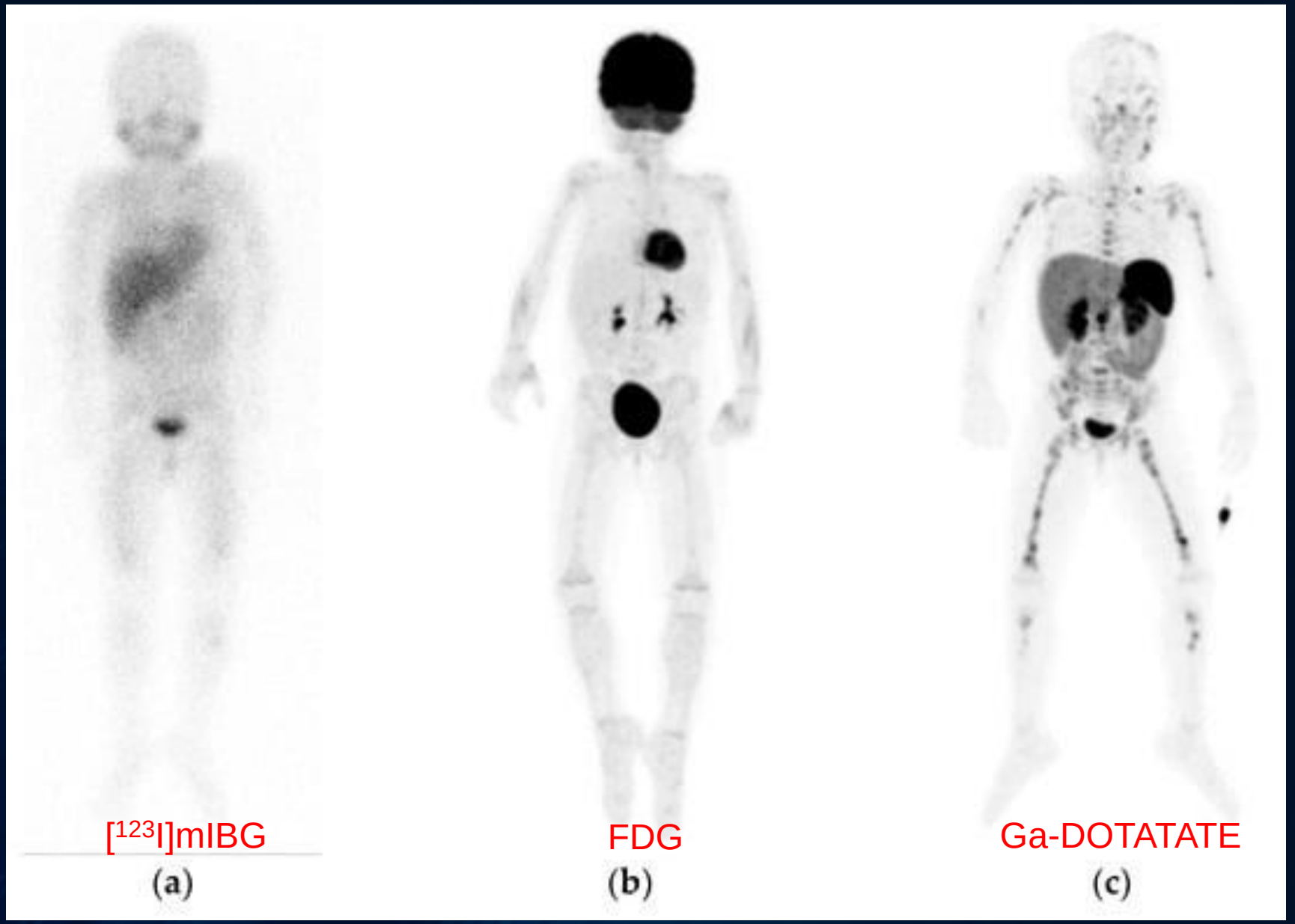
The challenge is to identify the patients for whom the benefits of **131I** therapy outweigh the risks.

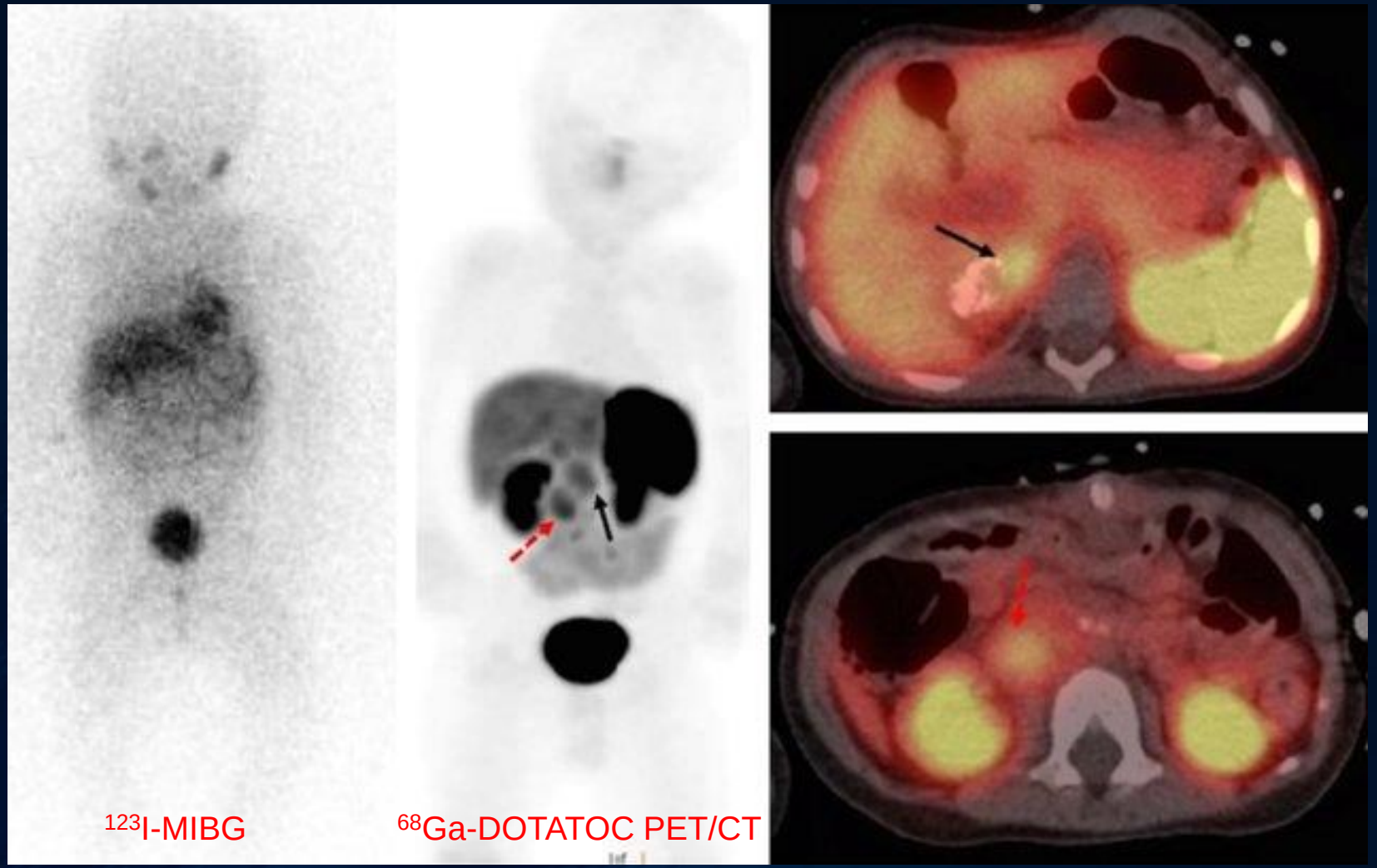
Neuroblastoma is the most common extracranial solid tumor in children, and is regarded as the most common malignant tumor in infants so far.

MIBG is an analog of guanethidine that shares features with norepinephrine and binds to the norepinephrine transporter.

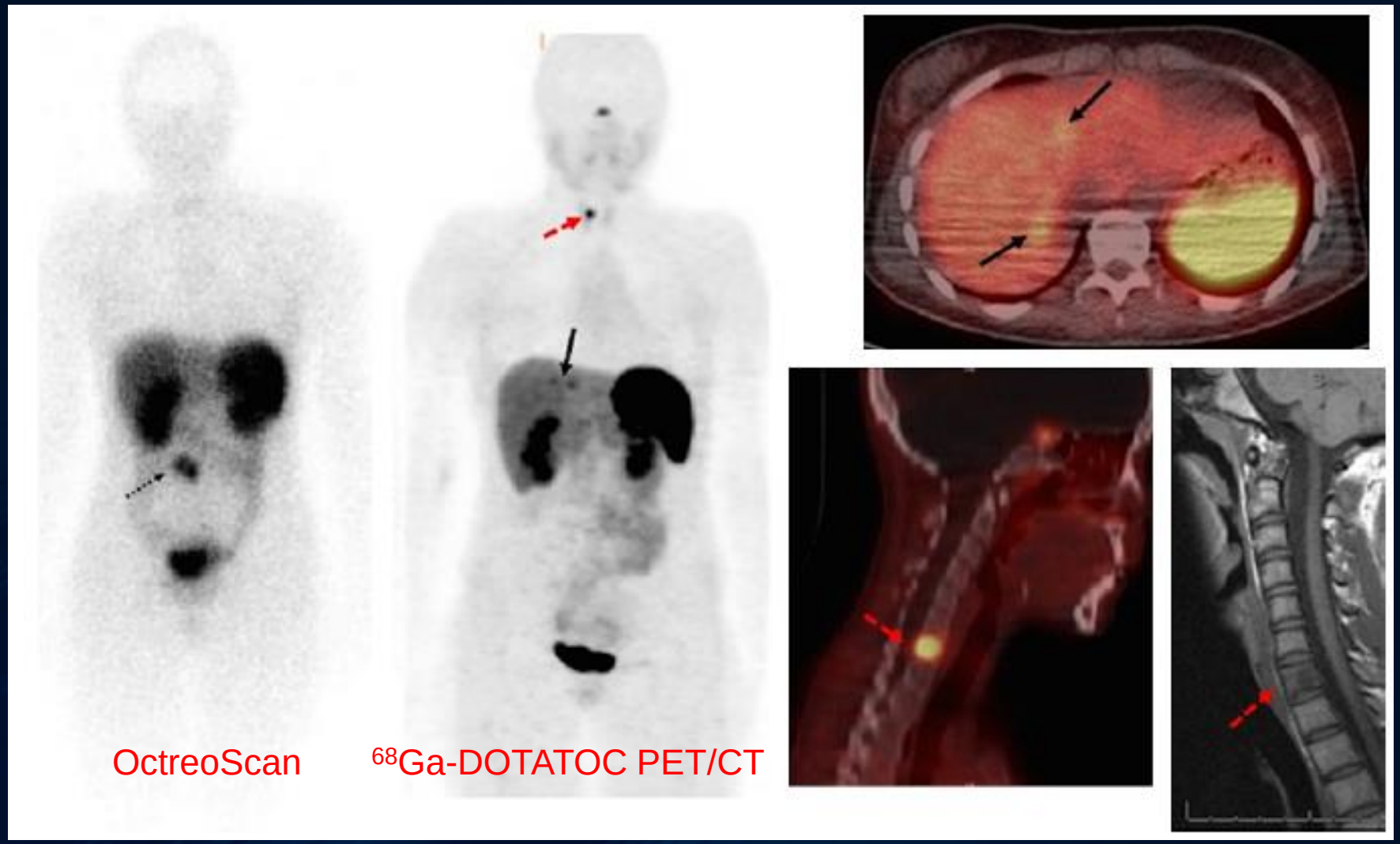
Radiolabeled MIBG is useful for imaging a variety of neuroendocrine tumors (NET) with higher sensitivity for tumor detection in PHEO,PARA and neuroblastoma than for other NET. Given the excellent localization typically seen in these tumors, therapy with **I-131 MIBG** is often feasible.

Standard
Prognostic
Theragnostic





A 17-month old patient with neuroblastoma



A 16-year old patient with small bowel NET

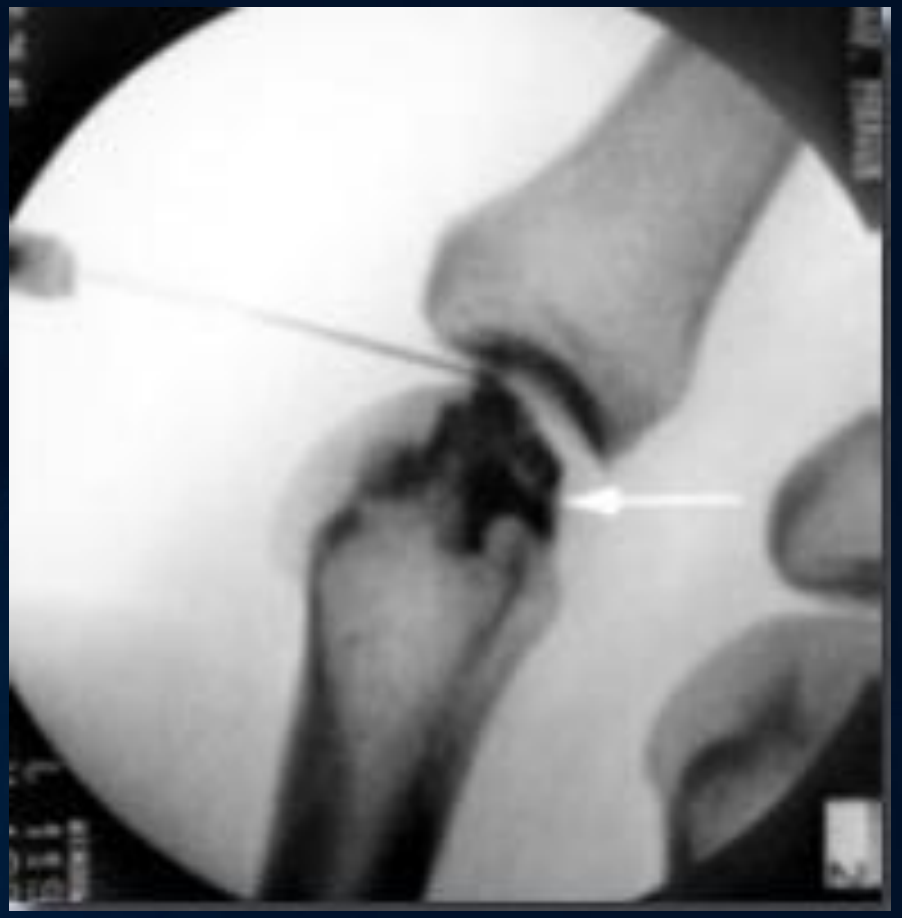
^{68}Ga-SSTR PET/CT is clearly superior over ^{99m}Tc-Octreotide or ^{123}I-MIBG scan.

Most importantly, the demonstration of **SSTR** avidity of a variety of pediatric tumors opens a new therapeutic option for children with peptide receptor radiotherapy (**PRRT**) for refractory solid tumors that express somatostatin receptor type II.

^{177}Lutetium-DOTATATE molecular radiotherapy can be used for;

- Neuroblastoma (Primary Refractory/Relapsed High-Risk),
- Metastatic NETs,
- Metastatic radioiodine-negative DTC and …

Radiosynovectomy



Future Directions

- ✓ Radioimmunotherapy,
- ✓ Alpha therapy,
- ✓ FAPI based imaging/therapy.

Preserve! Prevent! Prolong!
(Embrace these as the goals of care)

✓ **We all hope we can cure all cancers one day …**

- Preserve refers to maintaining a good quality of life and function,
- Prevent refers to using treatments of many modalities to avoid disease-related complications,
- Prolong should be obvious. The treatments we use don’t cure patients but they can lead to meaningful prolongations of life.