

***RADIONUCLIDE THERAPY OF  
DIFFERENTIATED THYROID  
CARCINOMA***

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# ***MANAGEMENT OF DTC***

## **1. Initial treatment**

### **1. Surgery**

**(thyroid surgery and LN surgery)**

### **2. Radioiodine ablation**

## **2. Follow-up**

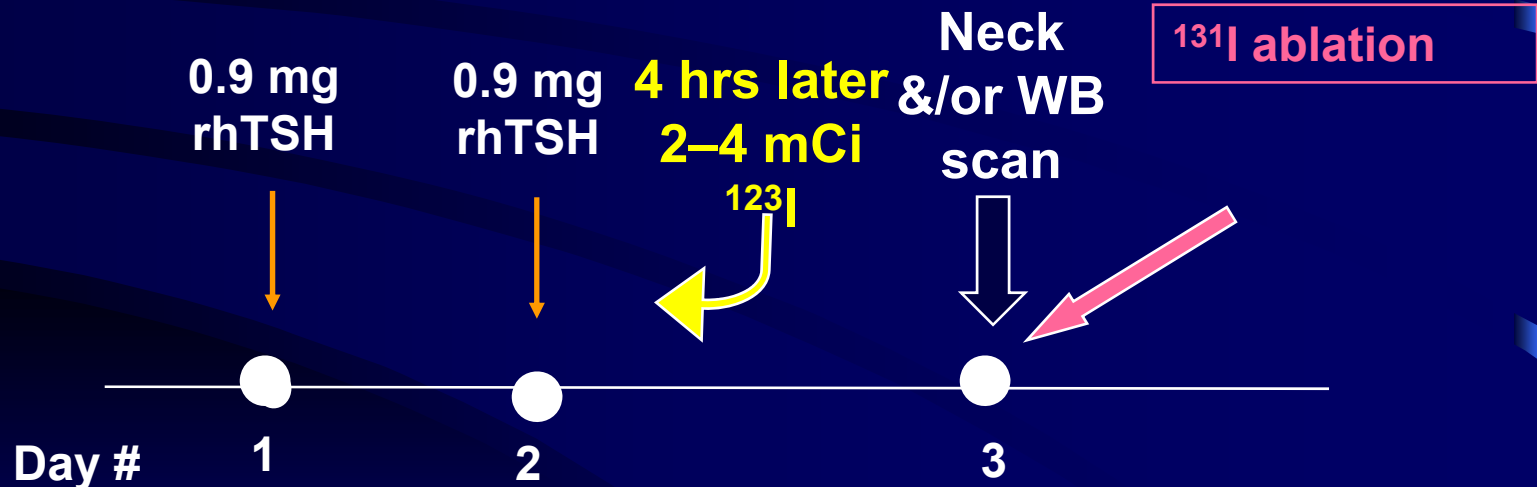
# I-131 THERAPY

- Preparation

- Low iodine diet [salt, sea food, supplements, red dye]
- Withdraw T4; substitute T3
- Withdraw T3; allow 2 weeks
- Assess clinically; confirm TSH > 30 mIU/L

# rhTSH- Thyrogen

Maintain  
Thyroid Hormone Therapy



# I-131 Therapy Dose Selection

Dose based on extent of disease

- Remnant ablation: 30,000 cGy
- Lymph Nodes 8,000-10,000 cGy

30 mCi to 75 mCi [1110-2800 MBq] vs Dosimetry

- Local disease: 100 -150 mCi [3.7 – 5.5 GBq]
- Lung, distal metastases: 60,000 cGy

Fixed dose: 150-200 mCi [5.5 – 7.2 GBq]

**Maximal Tolerated Dose:**

>200 mCi to 350-500 mCi [ $> 7.2$  18.5 GBq]

# Dosimetry in Patients with Thyroid Carcinoma

- Ablation is achieved if radiation dose exceeds 300 Gy. It allows more precise determination of  $^{131}\text{I}$  for efficient ablation.
- Dosimetry is simply a method to determine the energy absorbed from radiation.
- It is possible to determine the radiation absorbed dose in thyroid remnants, lymph node metastases, distal mets [lung, bone and other]
- We can select the administered dose of a known radionuclide
- To determine the radiation absorbed dose, measure the uptake, turnover rate and the mass or volume of distribution

# Treatment of thyroid remnant:

- Pre-determined dose: **75 mCi <sup>131</sup>I**
- Determine radiation dose to remnant
  - Measure thyroid uptake at 24 & 48 (or other time points)
  - Estimate remnant weight (from scan)
  - Calculate dose using MIRD formula or Becker-Zanzonico application of Benua-Leeper formulation

$$\text{Dose (cGy)} = \frac{\text{Admin Activity [mCi]} \times \text{T1/2 eff [days]} \times \% \text{ uptake} \times K}{\text{Gland Weight [gms]}}$$

$$\text{Admin dose} = \frac{\text{Desired rad Dose} \times \text{Gland Wt [gms]} \times 6.67}{\text{T 1/2 eff} \times 24 \text{ hr uptake [\%]}}$$

# Determination of Administered Dose to Ablate Remnant

$$\text{mCi [admin]} = \frac{\text{cGy} \times \text{gm} \times 6.67}{T_{1/2\text{eff}} \text{ [days]} \times \% \text{ uptake}}$$

**Example:** Patient post total thyroidectomy. What is the appropriate admin. dose of I-131 to ablate a focal area estimated to be < 2 g? Uptake 6%.  $T_{1/2} = 4$  days

$$\text{Answer: mCi} = \frac{3 \times 10^4 \times 2}{4 \times 6} \times 6.67$$

$$= \frac{6 \times 10^4}{24} \times 6.67 = \frac{40}{24} \times 10^4 \text{ mCi} = 1.6 \times 10^4 \text{ mCi}$$

$$= 16 \text{ mCi}$$

Patient can be successfully ablated with <30 mCi I-131

# Radiation Dosimetry in Thyroid Cancer Therapy

- **Maximal Tolerated Dose**
  - **Based on estimating and limiting Bone Marrow radiation absorbed dose by calculating Blood dose**
  - **Based on clinical observations at MSKCC [Benua & Leeper]: No adverse bone marrow effects if do not exceed 200 cGy to blood [per year]**
  - **Permits Administered doses >200 mCi to 350-500 mCi or greater but also identifies patients who cannot receive 200 mCi safely**
  - **Limit lung residual activity to 80 mCi (3 GBq) at 24 hrs**

# Treatment of metastatic disease

- **Fixed dose method: 150-200 mCi  $^{131}\text{I}$  every 6 months during the first 2 years and thereafter annually until total ablation of residual uptake on post-therapy  $^{131}\text{I}$ -WBS.**

*There is no limit to the cumulative dose of  $^{131}\text{I}$  in M1 (risk of cancer and leukemia rises with higher cumulative doses). If there is no uptake on post-therapy  $^{131}\text{I}$ -WBS – any further RAI is useless*

- **Maximum Tolerated dose based upon clinical observation that marrow can tolerate 200 – 300 cGy/ annum**
- **Determine maximum radiation absorbed dose to fraction of blood volume in the bone marrow**
- **[classically ~20% Plasma Volume]**

- **Assumption: Marrow radiation absorbed dose following  $^{131}\text{I}$  is derived primarily from b radiation while  $^{131}\text{I}$  is in the blood; secondarily from g radiation throughout the body**
- **Therefore: Measure  $^{131}\text{I}$  in blood at 4, 24, 48 (and more) hrs and Count Whole Body at 4, 24, 48 (and more) hrs**
- **Calculate or use computer program to determine mCi [MBq] dose of  $^{131}\text{I}$  that will deliver 200 cGy to blood**
  - **Can exceed 200 cGy in extreme cases**

# ***TREATMENT OF LOCAL AND REGIONAL RECURRENCE***

**In 5-20% DTC during early years of follow-up**

**Recurrences in lymph nodes 60-75% of all neck recurrences;  
Recurrence in soft tissues or invading aero-digestive tract –  
< 10% of all neck recurrences.**

## **Treatment:**

- \* Surgery +  $^{131}\text{I}$**
- \* Radiation therapy (no  $^{131}\text{I}$  uptake, incomplete surgery, involvement of aero-digestive tract/soft tissue)**
- \* Radiation therapy + chemotherapy in extensive and not operable recurrences**

## **Survival**

**10-year survival rate after local and regional recurrences was 62% (Tubiana, et al. Cancer 1985.)**

# *TREATMENT OF DISTANT METASTASES*

## *Patients with higher risk of M1:*

- \* Younger pts (<16 years)
- \* Older pts (>45 years)
- \* Histologic subtypes: PTC (tall-cell, columnar-cell, diffuse sclerosing variants); FTC (widely-invasive and poorly-differentiated subtypes)
- \* Large tumors and tumors extended beyond thyroid capsule and with lymph node mets
- \* Pts underwent less extensive surgery than TT or NTT
- \* Pts with no post-surgical administration of  $^{131}\text{I}$  ablation

- \* Initial M1 appears at the time of diagnosis. Late M1 occur during the follow up period.
- \* Distant metastases occur late more often in patients with follicular carcinoma while M1-initial are detected more often in patients with papillary carcinoma. Disease-specific survival is not significantly different among patients with M1-intial and M1-late. The risk of death from M1 increased after the age of 45 years (Mihailovic et al, Nuc med Comm 2009)
- \* Location: 57% in lungs, 24% in bones

## Treatment

- \* Surgery in bone mets; not for multiple lung mets

## *Complementary treatment*

### *Radiation therapy*

In bone mets which are not operable and non  $^{131}\text{I}$  avid;  
RAI + EBRT; + another RAI (3-6 months later)

### *Chemotherapy*

In progressive metastatic disease refractory to  $^{131}\text{I}$   
- 33% response rate to doxorubicin;

### *Other options*

Interferon- $\alpha$ ; interleukin-2; somatostatin analogs

## Survival

- \* Overall survival rate at 10 years from the detection of M1 was 25-40% (*Schlumberger, Pacini. Thyroid tumors, 2006*)
- \* Probability of survival after appearance of M1 was 60.7% at 5 years, 51.2% at 10, and 38.4% at 15 and 20 years (*Mihailovic, et al. Cancer Biother & Radioph, 2007*)
- \* Survival rate at 10 years was 93% in pts who achieved CR, vs. 14% in pts who did not (*Schlumberger, Pacini. Thyroid tumors, 2006*)

# *Prognostic factors for survival:*

## *Age*

Younger patients (at the detection of M1) have a lower risk of cancer-related death than older patients.

## *Histology*

Poorly-differentiated FTC have lower survival rates than PTC or well-FTC.

## *<sup>131</sup>I uptake*

Positive <sup>131</sup>I uptake indicates favourable prognosis. The absence of <sup>131</sup>I uptake in distant mets is a predicting factor which significantly shortens the survival of the patients (*Mihailovic et al., Thyroid, 2009.*)

# *Prognostic factors for survival:*

## *Extent of disease*

**The risk of death is the highest in patients with macronodular lung metastases or multiple bone mets. The site of M1 (lungs or bones) has no independent prognostic impact, but the bulkiness of the lesions.**

# ***FOLLOW-UP***

**- 12 months after initial treatment**

**1. clinical examination**

**2. US**

**3. stimulated Tg**

**4.  $^{131}\text{I}$ -WBS**

# Stimulated Tg + US with cytology = high sensitivity

- ❖ **US** is preferred for detecting nodal recurrences in the central and lateral neck.
- ❖ Lymph node mets: round, hypoechoic, microcalcifications or cystic components, at Doppler are hypervascularized.
- ❖ **FNA**: PC and TG analysis of aspirate.  
LIMITATION in the mediastinal space (interference with bone and air).
- ❖ **Tg** and **TgAb**, should be measured in the same laboratory using the same assay

## **$^{131}\text{I}$ -WBS + *Stimulated Tg* = high specificity**

- ❖  **$^{131}\text{I}$ -WBS will detect uptake in 60% to 80% of DTC patients with clinical lymph node metastases.**
- ❖ **1/3 of recurrent DTC with rising serum Tg lost their iodine avidity and show negative WBS.**
- ❖ **In WBS negative patients detection of persistent or recurrent disease is possible with CT, MRI and PET/CT**

## Comparing to CT, MRI

1. Allows multiplane evaluation,
  2. Has better tissue contrast,
  3. Allows no radiation to reach the neck,
  4. Can be performed with a paramagnetic contrast agent that does not interfere with subsequent  $^{131}\text{I}$  therapy
- ❖ MRI helps in detecting mediastinal metastatic lymph nodes, especially non-iodine-avid mets  
*(Mihailovic et al, AJR, 2010)*

# PET/CT

- ❖ Since more than 15 years, FDG-PET (and later PET-CT) has proven to be a useful tool for the diagnosis of thyroid cancer, mainly with iodine negative metastases.
- ❖ Iodine positive metastases are easily diagnosed using the I-131 WBS
- ❖ Thyroglobuline positive and iodine negative metastasis caused diagnostic problems. Iodine positive mets are mainly negative with FDG-PET while iodine negative metastasis present increased FDG-uptake. This “flip-flop phenomenon” has been first described in the late 90ies.
- ❖ PET-CT is a useful tool for the evaluation of patients with iodine negative metastases.





Settings Registration



- Object vs Target
- Optional vs Object
- Optional vs Target

Object vs Target Matrix

Default

Optional vs Object Matrix

Default

- Data Selector
- Image Registration
- Flexible Display
- Hard Copy

AC\_CT, 26.3.2010

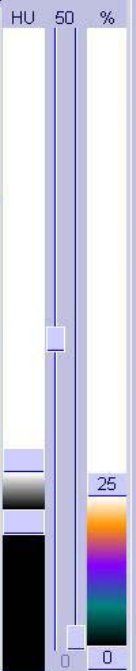
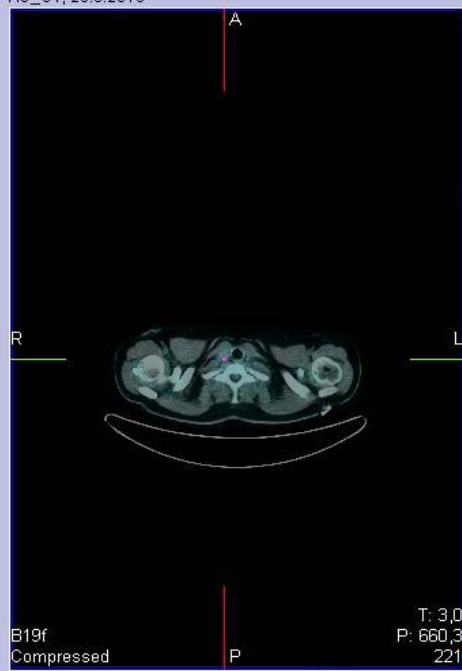
Transverse

Sagittal

Coronal

PET WB, 26.3.2010

HU 50 %



Transverse

Rotation Z 0

Sagittal

Rotation X 0

Coronal

Rotation Y 0

Translation (mm): X 0 Y 0 Z 0

Landmarks...

Complete Suspend Setup

## ***DIAGNOSTICS OF IODINE NON AVID METASTASES***

- 1. In a limited number of patients, iodine negative thyroid cancer may express somatostatin receptors.**
- 2. If this is the case, radiopeptide therapy may be performed.**
- 3. Ga-68 DOTATOC PET-CT may be helpful in the selection of these patients.**