Long term secondary effects of radioiodine (I-131)

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Belgian Thyroid Club meeting, November 27, 2010
Late effects of radioiodine (I-131)

Introduction: Efficacy

- I-131 is cost-efficient in treating benign thyroid disorders (nodular goiter, Graves disease and toxic adenoma).
- I-131 ablation after total thyroidectomy for DTC is efficient in reducing recurrence rate and mortality (?) of Stage >2 cancer and provides a way to use thyroglobulin as a specific tumor marker.
- I-131 is efficient in treating recurrence, residual disease after surgery and metastases of DTC.
- Because the prognosis is usually good, patients have many years to develop late sequelae.
Late effects of radioiodine (I-131)

Contents

• Introduction
• Effects on the salivary glands
• Effects on the lung
• Effects on the reproductive system
• Effects on the bone marrow
• Radiation-induced cancer
• Conclusions
Late effects of radioiodine (I-131)

Introduction: general safety

LIMITED ACUTE SIDE EFFECTS

No bone marrow depression
Gastritis (nausea, vomiting)
Sialadenitis, taste changes and caries
Hypospermia (amenorrhoea)
Radiation thyroiditis if incomplete surgery
Tumor swelling and metastatic flare (Cave CNS)

Acute autoimmune thyroiditis (with thyroid storm)
Worsening or induction of thyroid ophthalmopathy
Late effects of radioiodine (I-131)
Introduction: effects of thyroid irradiation
Late effects of radioiodine (I-131)

Introduction: effects of thyroid irradiation

CHERNOBYL
Incorporation 40,000 Bq ~ 1 mSv

8,000 Bq ~ 1 mGy

100-2,000 mGy = 5 to 100 times more thyroid cancer mainly in youngests

No deterministic effects, mainly stochastic effects

MEDICAL USE

Doses: 40,000-100,000 mGy (40-100 Gy) to the target organ
Activities: ~3,700,000,000 Bq (100 mCi and more in cancer)

Deterministic effects expected, delayed (stochastic) effects possible
Late effects of radioiodine (I-131)

Introduction: effects of radiation

**DETERMINISTIC EFFECTS**

Depend on threshold (>200mGy), shortly after exposure  
Probability and severity increase with dose  
Not avoidable, may or may not induce irreversible changes  
e.g. radiodermitis, lung fibrosis, bone marrow failure, brain damage...

**STOCHASTIC EFFECTS**

Concept of linear non-threshold effect, delayed 5-15 y  
Probability increases with dose, severity follows 0/1 rule  
Not avoidable but may be anticipated by screening  
i.e. cancer induction and hereditary effects (in offspring)
Late effects of radioiodine (I-131)

Introduction: effects of « radiation »

- Sunburn: deterministic
- Melanoma: stochastic
Late effects of radioiodine (I-131)
Effects on salivary glands

- Doses from I-131 to the salivary (and lacrymal) glands can be high, up to 15 Gy
- Sialadenitis and persistent xerostomia occur in up to 22%
- Dry eyes and conjunctivitis are less frequent

Alexander et al. JNM 1998
Late effects of radioiodine (I-131)
Effects on salivary glands

Solans et al. JNM 2001

Nakada et al. JNM 2005

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TABLE 1
Incidence of Lacrimal and Salivary Gland Dysfunction in 79 Patients After Radioiodine Therapy

<table>
<thead>
<tr>
<th>Event</th>
<th>First year n (%)</th>
<th>Second year n (%)</th>
<th>Third year n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjective xerostomia</td>
<td>26 (32.9%)</td>
<td>16 (20.3%)</td>
<td>12 (15.2%)</td>
</tr>
<tr>
<td>New cases*</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Objective xerostomia</td>
<td>40 (50.6%)</td>
<td>11 (13.9%)</td>
<td>11 (13.9%)</td>
</tr>
<tr>
<td>Stage 2</td>
<td>24</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Stage 3</td>
<td>16</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Stage 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New cases*</td>
<td>3 (3.8%)</td>
<td>28 (35.4%)</td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>3</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Stage 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subjective xerophthalmia</td>
<td>20 (25.3%)</td>
<td>14 (17.7%)</td>
<td>11 (13.9%)</td>
</tr>
<tr>
<td>New cases*</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Objective xerophthalmia</td>
<td>14 (17.7%)</td>
<td>11 (13.9%)</td>
<td>6 (7.6%)</td>
</tr>
<tr>
<td>Schirmer test</td>
<td>14</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Rose Bengal dye</td>
<td>8</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Tear break-up time</td>
<td>10</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>New cases*</td>
<td>2 (2.5%)</td>
<td>2 (2.5%)</td>
<td></td>
</tr>
<tr>
<td>Schirmer test</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Rose Bengal dye</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Tear break-up time</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

---

TABLE 2
Comparison of Incidence of Salivary Side Effects After High-Dose Radioiodine Therapy Between Group A and Group B

<table>
<thead>
<tr>
<th>Event</th>
<th>Incidence* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (n = 105)</td>
</tr>
<tr>
<td>Sialoadenitis</td>
<td>63.8 (67/105)</td>
</tr>
<tr>
<td>Taste dysfunction</td>
<td>39.0 (41/105)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>23.8 (25/105)</td>
</tr>
<tr>
<td>Xerostomia</td>
<td>14.3 (15/105)</td>
</tr>
</tbody>
</table>

*Values in parentheses are numbers of patients.
Late effects of radioiodine (I-131)  
Effects on the lung

- Lung toxicity may occur over 30 Gy (fibrosis)
- Definite differentiation between DTC- and fibrosis-related lung restriction is impossible (Samuel, 1998)
- This can only occur in patients with diffuse lung metastases, i.e. who may take up a cumulative activity > 80 mCi (Benua et al. 1962, 1986)
Late effects of radioiodine (I-131)
Effects on the lung

- Mortality in such patients was reported as early as in 1957 (Rall et al. JCEM)

- Limiting a single dose to less than 200 mCi enables repair mechanisms to avoid severe toxicity. Very high doses however are associated with unavoidable lung toxicity (e.g. over 1000 mCi with diffuse lung disease), including in children (Cecarelli et al. Surgery 1988, Reiners et al. EJNM, 2003)

See letter by Chen et al. Thyroid, 2010, Schlumberger et al. JNM 1988
Late effects of radioiodine (I-131)
Effects on the reproductive function

- Doses to gonads vary between 5 and 200 mGy, depending on administered activities. Such doses are not suppressive of gonadal function.

- In males, doses up to 200 mGy may result in:
  - transient oligo(a)zoospermia
  - decreased testosterone secretion
  - full recovery at one year

Sperm banking has been advocated as a precaution but not substantiated.
Hyer et al. Clin Endocrinol 2002
Late effects of radioiodine (I-131)
Effects on the reproductive function

**Fig. 2.** Serum inhibin B levels before (25 patients) and 3 (11 patients), 6 (18 patients), 12 (22 patients) and 18 months (18 patients) after the last $^{131}$I therapy. The horizontal line shows the lower normal limit. Vertical bars indicate the SEM. Statistical results, using ANOVA and Student’s $t$ test, are shown at the top.

**Fig. 5.** Serum testosterone/LH ratio before (25 patients) and 3 (11 patients), 6 (18 patients), 12 (22 patients) and 18 months (18 patients) after the last $^{131}$I therapy. The horizontal line shows the lower normal limit. Vertical bars indicate the SEM. Statistical results, using ANOVA and Student’s $t$ test, are shown at the top.

Testicular function after radioiodine therapy for thyroid carcinoma

Late effects of radioiodine (I-131)
Effects on the ovarian function

- Therapeutic doses of I-131 may result in transient amenorrhoea lasting for up to 15 months (raised FSH)
- Disturbances of the menstrual cycles increase with the dose
- Menopause is observed slightly earlier in patients treated with I-131 (not an effect of autoimmunity)

Cecarelli et al. JCEM 2001
Median age at treatment: 40y
Late effects of radioiodine (I-131) Effects on fertility

• There is hardly any evidence that small (10 mCi) to large (hundreds of mCi) activities of I-131 impair fertility
• Fertility rate (n babies/n year fertility *1000) was 23 in females treated with I-131 (2.6-22.2 GBq) vs 19 in those who were not (surgery only) (Dottorini et al. JNM 1995)
• Conception success is high (Vini et al. Postgrad Med J 2002) (4 premature and 14 miscarriages, no fetal abnormality)
Late effects of radioiodine (I-131) 
Effects on fertility

• One study suggested that the rate of miscarriage raised during the first year following I-131 (Schlumberger et al. JNM 1996), but the impact of hypothyroidism was not assessed

• In the largest series on **2673 pregnancies in 1126 patients**, there were no increased risks related to I-131 of:
  - miscarriage
  - congenital abnormalities and related cancer in offspring
  - stillbirth
  - low birth weight and prematurity

  Garsi et al. JNM 2008
Late effects of radioiodine (I-131) 
Effects on fertility

<table>
<thead>
<tr>
<th>Factor (overall population)</th>
<th>No. of pregnancies</th>
<th>Miscarriages</th>
<th>Stillbirths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Before any treatment</td>
<td>1,857</td>
<td>193</td>
<td>10.4</td>
</tr>
<tr>
<td>After surgery for thyroid cancer</td>
<td>475</td>
<td>92</td>
<td>20.7</td>
</tr>
<tr>
<td>Cumulative radioiodine activity before conception (MBq)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>86</td>
<td>17</td>
<td>19.8</td>
</tr>
<tr>
<td>&lt;370</td>
<td>152</td>
<td>28</td>
<td>18.4</td>
</tr>
<tr>
<td>370–3,700</td>
<td>59</td>
<td>9</td>
<td>15.3</td>
</tr>
<tr>
<td>&gt;3,700</td>
<td>178</td>
<td>38</td>
<td>21.4*</td>
</tr>
<tr>
<td>Radiiodine activity during year before conception (MBq)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>366</td>
<td>69</td>
<td>18.9</td>
</tr>
<tr>
<td>&lt;370</td>
<td>93</td>
<td>20</td>
<td>21.5</td>
</tr>
<tr>
<td>≥370</td>
<td>16</td>
<td>3</td>
<td>18.8</td>
</tr>
</tbody>
</table>

*P < 0.05, as determined by $\chi^2$ test for heterogeneity.

Garsi et al. JNM 2008
Late effects of radioiodine (I-131)
Effects on fertility

Garsi et al. JNM 2008

### TABLE 5
Outcomes of 2,009 Live Births as Function of Radioiodine Exposure

<table>
<thead>
<tr>
<th>Factor (overall population)</th>
<th>Radiation dose, in mGy, to ovaries (range)</th>
<th>No. of live births</th>
<th>% of girls</th>
<th>% (no.) with:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Term of &lt;37 wk</td>
</tr>
<tr>
<td>Before any treatment</td>
<td>1,633 (range)</td>
<td>49.3</td>
<td>7.0 (114)</td>
<td>10.3 (168)</td>
</tr>
<tr>
<td>After surgery for thyroid cancer</td>
<td>376 (range)</td>
<td>45.3</td>
<td>12.8 (44)</td>
<td>8.6 (33)</td>
</tr>
</tbody>
</table>

Cumulative radioiodine activity before conception (MBq)

<table>
<thead>
<tr>
<th>Radiation dose (MBq)</th>
<th>No. of live births</th>
<th>% of girls</th>
<th>% (no.) with:</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>40.6</td>
<td>6.0</td>
</tr>
<tr>
<td>&lt;370</td>
<td>7 (0–13)</td>
<td>50</td>
<td>11.6</td>
</tr>
<tr>
<td>370–3,700</td>
<td>85 (14–140)</td>
<td>40.8</td>
<td>4.1</td>
</tr>
<tr>
<td>&gt;3,700</td>
<td>305 (141–1,443)</td>
<td>45</td>
<td>17.3</td>
</tr>
</tbody>
</table>

Radiiodine activity during year before conception (MBq)

<table>
<thead>
<tr>
<th>Radiation dose (MBq)</th>
<th>No. of live births</th>
<th>% of girls</th>
<th>% (no.) with:</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>46.6</td>
<td>12.8</td>
</tr>
<tr>
<td>&lt;370</td>
<td>3.92</td>
<td>39.7</td>
<td>12.3</td>
</tr>
<tr>
<td>≥370</td>
<td>144.2</td>
<td>46.2</td>
<td>15.4</td>
</tr>
</tbody>
</table>
Late effects of radioiodine (I-131)
Effects on the bone marrow

- Bone marrow dose remain usually low (0.2-1 Gy)
- The LD5/5 to the bone marrow is 3 Gy
- Low activities (< 200 mCi) are not associated with clinically relevant BM depression
- High activities may induce transient BM depression, especially if previous therapies have already occurred
- Preparation with rh-TSH, by reducing the whole-body dose allows higher doses to tumours while sparing the BM (de Keizer et al. JNM 2004)
Late effects of radioiodine (I-131) Effects on the bone marrow

Dorn et al. JNM 2003: High-dose RAI based on pretherapeutic dosimetry aiming at >100 Gy to metastases, < 3 Gy to BM and < 30 Gy to lungs, up to 900 mCi
Late effects of radioiodine (I-131) 
Effects on the bone marrow

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Pretreatment platelet count (×10^9/L)</th>
<th>3-mo posttreatment platelet count (×10^9/L)</th>
<th>Change between pretreatment and 3-mo counts (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>203</td>
<td>158</td>
<td>-22</td>
</tr>
<tr>
<td>2</td>
<td>306</td>
<td>251</td>
<td>-16</td>
</tr>
<tr>
<td>3</td>
<td>197</td>
<td>152</td>
<td>-23</td>
</tr>
<tr>
<td>4</td>
<td>283</td>
<td>233</td>
<td>-16</td>
</tr>
<tr>
<td>5</td>
<td>172</td>
<td>140</td>
<td>-19</td>
</tr>
<tr>
<td>6</td>
<td>175</td>
<td>146</td>
<td>-17</td>
</tr>
<tr>
<td>7</td>
<td>316</td>
<td>400</td>
<td>+27</td>
</tr>
<tr>
<td>8</td>
<td>264</td>
<td>306</td>
<td>+16</td>
</tr>
<tr>
<td>9</td>
<td>210</td>
<td>203</td>
<td>-3</td>
</tr>
<tr>
<td>10</td>
<td>154</td>
<td>165</td>
<td>+7</td>
</tr>
<tr>
<td>11</td>
<td>338</td>
<td>343</td>
<td>+1</td>
</tr>
<tr>
<td>12</td>
<td>236</td>
<td>196</td>
<td>-17</td>
</tr>
<tr>
<td>13</td>
<td>305</td>
<td>337</td>
<td>+10</td>
</tr>
<tr>
<td>14</td>
<td>NP</td>
<td>NP</td>
<td>-</td>
</tr>
<tr>
<td>15</td>
<td>NP</td>
<td>NP</td>
<td>-</td>
</tr>
<tr>
<td>16</td>
<td>NP</td>
<td>NP</td>
<td>-</td>
</tr>
<tr>
<td>17</td>
<td>NP</td>
<td>NP</td>
<td>-</td>
</tr>
</tbody>
</table>

*Patient received 3 rhTSH-aided treatments.
*Patient received 2 rhTSH-aided treatments.
NP = not performed.

Metastatic patients 200 mCi after rh-TSH (de Keizer et al. JNM 2004)
Late effects of radioiodine (I-131) Leukemia

- It is expected to find a clear dose relationship between BM irradiation and the incidence of leukemia (from atomic bomb survivors > 400 mGy)
- In spite of this, no excess incidence of leukemia was found in the largest registry (Hall et al. Lancet 1992)
  - Diagnostic I-131 (dose: 0.19 mGy, SIR 1.16)
  - Hyperthyroidism (dose: 48 mGy, SIR 0.81)
  - Thyroid cancer (dose: 251 mGy, SIR 2.37)

(excess observed only for CLL [not radiation-induced, 4 cases] with doses over 100 mGy)
Late effects of radioiodine (I-131)
Leukemia

- Data from a large international (Fr+Sw+It) database show (Rubino et al. Br J Cancer 2003)

  Increased incidence of leukemia (12 vs 6) among 6841 thyroid cancer patients (mean activity 6 GBq [0.2-55.5]). Risk is 0.8 case/GBq/10000 PYR, i.e. an excess 3/10 yr due to Rx

  Effect seems more pronounced in patients with external radiotherapy, but this is not significant

  Individual databases did not provide any evidence and subclassification of leukemias is not provided
Late effects of radioiodine (I-131)
Secondary primary malignancy

- Conclusions from the largest collected data (Sawka et al., Thyroid 2009)
  - 16,502 pts with DTC, among which 8,473 treated with RAI
  - Combined European* and American (SEER)** databases
  - RR (incidence) of all malignancies is 1.19 ($P=0.01$)
  - RR for leukemia is 2.5 ($P=0.024$)
  - No increased incidence for all other organs

Interestingly, the RR for leukemia is in the same range as for breast cancer survivors treated with radiotherapy

*Rubino et al (mean activity 6 GBq) **Brown et al. JCEM 2008
Late effects of radioiodine (I-131)  
Secondary primary malignancy

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*Rubino et al (mean activity 6 GBq)  **Brown et al. JCEM 2008
Late effects of radioiodine (I-131) Secondary primary malignancy

1571 Abstracts obtained from electronic search + 36 full-text references from other sources = total of 1607 unique references screened by 2 reviewers

172 Full-text relevant studies reviewed in detail

23 excluded since primary malignancy was not thyroid
14 excluded since no data on second primary malignancies
27 excluded since no new data (commentary, narrative review)
39 excluded since case report or case series of <50 individuals
14 excluded since no control comparison
15 excluded since not English
10 excluded since duplicate publications
28 excluded since no relative risk or insufficient data to calculate risk of second malignancy after radioactive iodine
Late effects of radioiodine (I-131)
Secondary primary malignancy

- Studies comparing with general population had shown:
  - Slightly increased incidence (or mortality) of stomach, lung (hyperthyr.), urinary bladder, brain (hyperthyr.), thyroid (nodular goiter and hyperthyroidism), myeloid malignancies, etc...
  - Some studies showed a reduced risk for some cancers... leading to globally unchanged total incidence and mortality
  - Unexpectedly, dose-relationships could not be proven
Late effects of radioiodine (I-131)
Secondary primary malignancy

• Large study *in hyperthyroidism* (Ron et al. JAMA 1998) showed:
  - no excess in overall cancer mortality
  - small excess for thyroid, lung, breast and kidney cancer
  - only thyroid cancer is related to RAI

### Table 2.—Selected Characteristics of Study Population by Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Female, No. (%)</th>
<th>Male, No. (%)</th>
<th>Total, No. (%)</th>
<th>Age, Mean, y</th>
<th>Follow-up, Mean, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodine 131</td>
<td>18 020 (63.8)</td>
<td>5 000 (68.1)</td>
<td>23 020 (64.7)</td>
<td>49.0</td>
<td>18.9</td>
</tr>
<tr>
<td>Iodine 131 only</td>
<td>7 029 (24.9)</td>
<td>1 999 (27.2)</td>
<td>8 028 (25.4)</td>
<td>49.9</td>
<td>18.0</td>
</tr>
<tr>
<td>Iodine 131 and drugs</td>
<td>7 999 (28.3)</td>
<td>2 440 (33.2)</td>
<td>10 439 (29.3)</td>
<td>49.5</td>
<td>18.5</td>
</tr>
<tr>
<td>Iodine 131 and surgery</td>
<td>757 (2.7)</td>
<td>135 (1.8)</td>
<td>892 (2.5)</td>
<td>48.3</td>
<td>19.7</td>
</tr>
<tr>
<td>Iodine 131 and surgery and drugs</td>
<td>2 235 (7.9)</td>
<td>426 (5.8)</td>
<td>2 661 (7.5)</td>
<td>44.5</td>
<td>23.1</td>
</tr>
<tr>
<td>Surgery (no iodine 131)</td>
<td>9 119 (32.3)</td>
<td>2 080 (28.3)</td>
<td>11 199 (31.5)</td>
<td>41.6</td>
<td>26.2</td>
</tr>
<tr>
<td>Surgery only</td>
<td>654 (2.3)</td>
<td>164 (2.2)</td>
<td>818 (2.3)</td>
<td>50.8</td>
<td>22.7</td>
</tr>
<tr>
<td>Surgery and drugs</td>
<td>8 465 (30.0)</td>
<td>1 916 (26.1)</td>
<td>10 381 (29.2)</td>
<td>40.8</td>
<td>26.5</td>
</tr>
<tr>
<td>Drugs only</td>
<td>1 094 (3.9)</td>
<td>260 (3.6)</td>
<td>1 354 (3.8)</td>
<td>44.9</td>
<td>17.8</td>
</tr>
<tr>
<td>Total†</td>
<td>28 248 (100.0)</td>
<td>7 345 (100.0)</td>
<td>35 593 (100.0)</td>
<td>46.5</td>
<td>21.2</td>
</tr>
</tbody>
</table>
Late effects of radioiodine (I-131)
Secondary primary malignancy

Points of controversy

- breast cancer incidence increased in French patients treated for DTC, but NOT in those treated with RAI (Adjadj et al. Cancer 2003)

- an association of thyroid cancer was found (SEER, 2,036,597 pts) with a number of cancers, irrespective of which occurred first (breast without any relationship with RAI and CLL with a two-fold increase, although not being a radiation-induced cancer) (Ronkers et al. Int J Cancer 2005)

- These findings suggest etiologic similarities and a possible ‘general’ therapeutic effect
Late effects of radioiodine (I-131)
Secondary primary malignancy

DNA repair foci after $^{131}$I therapy
$\sim$100 mCi, 0.3 Gy to blood
Lassmann et al. JNM 2010
Late effects of radioiodine (I-131)
Secondary primary malignancy

Frigo et al. JCEM 2009
Late effects of radioiodine (I-131)  
Conclusions (1)

• Severe effects following radioiodine therapy are rare even after very high doses

• **Deterministic effects:**
  - Mainly lung (metastatic) and salivary glands (physiological)
  - Little if any permanent effect on the reproductive system
  - No significant effect on fertility and offspring

• **Stochastic effects:** Radiation-induced cancer remains limited but must be kept in mind (essentially solid cancer)
Late effects of radioiodine (I-131)  
Conclusions (2)

- **Adequate preparation** is required (hydration, laxatives, lemon juice, contraception, pregnancy test,...) to limit the radiation dose to normal tissues

- Because whole-body doses are reduced preparation with **rh-TSH** instead of thyroxine withdrawal may reduce long-term side effects and proved effective in reducing acute BM toxicity for patients treated with high activities

- **Pre-therapeutic dosimetry** is now recommended for patients treated with high activities (e.g. metastatic patients)

- Biological dosimetry is an attractive tool for assessing effects and risks (this remains to be assessed on the long term)
Late effects of radioiodine (I-131) Leukemia

Rubino et al. Br J Cancer 2003

But the French and Italian databases did not provide any case in previous publications

<table>
<thead>
<tr>
<th>Type of SPM</th>
<th>Amount of $^{131}$I (GBq)</th>
<th>Number of SPM/PYR</th>
<th>RR$^a$ (95% CI)</th>
<th>Number of SPM/PYR</th>
<th>RR$^a$ (95% CI)</th>
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<td>Solid cancers</td>
<td>≤0.2 [0.2–3.6] [3.7–7.3] [7.4–14.7]</td>
<td>186/29625</td>
<td>1 (ref)</td>
<td>84/10629</td>
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<td>[7.4–14.7]</td>
<td>12/1475</td>
<td>1.5 (0.8–2.6)</td>
<td>7/495</td>
<td>2.1 (0.9–4.7)</td>
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<td>Leukaemias</td>
<td>≤0.2 [0.2–3.6]</td>
<td>4/29625</td>
<td>1 (ref)</td>
<td>2/10629</td>
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<td>2.2 (0.1–23.5)</td>
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<td>4/19644</td>
<td>2.6 (0.5–11.8)</td>
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<td>≥18.5</td>
<td>0/853</td>
<td>–</td>
<td>1/372</td>
<td>14.0 (0.6–167.4)</td>
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