A Review of Thyroid Cancer and Follow up Screening after Initial Treatment

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Summary

- This paper presents a cost-effective and simple screening method to follow up thyroid cancer patients who have had their thyroid surgically removed (thyroidectomy), without any metastases, and have been declared stable or cured.
- The method is based on using a small NaI (Tl) detector system and oral intake of $^{131}$I, to measure the concentrated radioactive iodine uptake (RAIU), together with measurements of blood levels of protein Thyroglobulin (Tg).
Vietnam, with a population of nearly 97 Million inhabitants in 2018, has one of the highest rate of cancer fatalities according to the World Health Organisation (WHO).

The 5-year prevalence (all ages) of all cancer sites is 300 000, and the number of new cancer cases during January - November 2018 was 165 000.

The rate of patients who recover from cancer treatment in Vietnam is only 30% - 40%, compared to 70% - 80% in many developed countries.

Vietnam ranks third in the world with the number of male cancer cases at 135 – 178 patients for every 100,000 men.

The mortality rate of Vietnamese male cancer patients is among the highest in the world, with an age-standardized mortality rate* of 146.

The majority of the population, especially men, neglect their health and tend to ignore the symptoms.

Diagnosis and treatment are not easily available to everyone.

Diagnosis and treatment of cancer only occurs in the latter stages of the disease in over 70% of the cases, when the probability of successful treatment is less.

* The age-standardized mortality rate a weighted average of the age-specific mortality rates per 100,000 persons, where the weights are the proportions of persons in the corresponding age groups of the WHO standard population.
Thyroid Gland

- Thyroid gland is part of the endocrine system, which regulates hormones in the body.
- The thyroid gland absorbs iodine from the bloodstream to produce thyroid hormones, which regulate a person's metabolism.
- A normal thyroid gland has two lobes, one on each side of the windpipe joined by a narrow strip of tissue called the isthmus.

Thyroid Cancer

- Most thyroid cancers can be cured, especially if they are found at an early stage and they have not created metastases.
- After the thyroid cancer is found and staged, the treatment is chosen. The main treatment methods for thyroid cancer is:
  - Surgery, followed by radioactive iodine ($^{131}$I) treatment.
  - After that hormone treatment due to no thyroid gland.
There are four main types of thyroid cancer:

1. Papillary thyroid cancer (PTC)
   - PTC develops from the follicular cells and grows slowly.
   - Most common type of thyroid cancer.
   - It is usually found in one lobe; only 10% - 20% of papillary thyroid cancers appear in both lobes.
   - A differentiated thyroid cancer, meaning that the tumor looks similar to normal thyroid tissue under a microscope.

2. Follicular thyroid cancer (FTC)
   - FTC also develops from the follicular cells and usually grows slowly.
   - It is also a differentiated thyroid cancer, but it is less common than PTC.
   - PTC and FTC are both very often curable, especially when found early and in people younger than 45 years old.
   - Together, papillary and follicular thyroid cancers make up about 90% of all thyroid cancers cases.
3. Medullary thyroid cancer (MTC)

- MTC develops in the C cells and is sometimes the result of a genetic syndrome called multiple endocrine neoplasia type 2.
- This tumor has very little, if any, similarity to normal thyroid tissue.
- MTC can often be controlled if it is diagnosed and treated before it spreads to other parts of the body.
- MTC accounts for about 5% of thyroid cancers.

4. Anaplastic thyroid cancer (ATC)

- This type of thyroid cancer is rare, and only accounts for about 2% of all thyroid cancers.
- It is a fast-growing, poorly differentiated thyroid cancer that starts from differentiated thyroid cancer or a benign tumor of the gland.
- Because this type of cancer grows so quickly, it is more difficult to treat successfully.

*Thyroid cancer cells further differentiate with time, which means that detection of thyroid cancer at an early stage is extremely important to increase the cure rate and limiting sequelae, complications of surgical treatment and radiation therapy!*
Radiation Dosimetry

Estimated absorbed radiation doses to an average (70 kg) euthyroid (normal functioning thyroid gland) patient from an oral dose of 5 mCi $^{131}$I in milligray (mGy) per megabecquerel (MBq), and rad per millicurie (mCi).

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Thyroid Uptake</th>
<th>5%</th>
<th>15%</th>
<th>25%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mGy/MBq</td>
<td>MBq</td>
<td>mGy/MBq</td>
<td>MBq</td>
</tr>
<tr>
<td>Thyroid</td>
<td>22</td>
<td>200</td>
<td>300</td>
<td>1200</td>
</tr>
<tr>
<td>Stomach</td>
<td>0.45</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Red Marrow</td>
<td>0.038</td>
<td>0.07</td>
<td>0.20</td>
<td>0.36</td>
</tr>
<tr>
<td>Liver</td>
<td>0.03</td>
<td>0.11</td>
<td>0.12</td>
<td>0.035</td>
</tr>
<tr>
<td>Testes</td>
<td>0.029</td>
<td>0.10</td>
<td>0.027</td>
<td>0.10</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.044</td>
<td>0.16</td>
<td>0.043</td>
<td>0.16</td>
</tr>
<tr>
<td>Testes</td>
<td>0.03</td>
<td>0.11</td>
<td>0.032</td>
<td>0.12</td>
</tr>
<tr>
<td>Liver</td>
<td>0.03</td>
<td>0.11</td>
<td>0.12</td>
<td>0.035</td>
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</tr>
</tbody>
</table>

• Patients who have been diagnosed with thyroid cancer, and who have had surgery thyroidectomy, will undergo a planar scintigraphy head and neck scan 6-8 weeks after surgery to visualize the location and the amount of any remaining thyroid remnant and possibly thyroid cancer.

• Two days before the planar scan, the patients should take 2 mCi $^{131}$I orally.

• Prior to the $^{131}$I treatment, the patients have to follow a low iodine diet for 1-2 weeks to deplete their body of iodine, and the thyroid stimulating hormone (TSH) should be higher than 30 mIU/L.

• After undergoing the planar head and neck scan, the patients will be given $^{131}$I orally and remain in the hospital for 3-4 days. After 7-10 days, the patients will be asked to return to the hospital for a whole body scan (WBS) using single photon emission computed tomography (SPECT), which shows where the $^{131}$I was deposited in the body. This scan may also identify any new sites of iodine-avid thyroid cancer not seen during the first WBS.
After one month, the patients should return to the hospital to check blood levels of TSH, FT4, Tg, TgAb and to adjust the levothyoxine (a manufactured form of the thyroid hormone thyroxine) dosage.

After around 6 months, the patients should return to the hospital again to be given 5 mCi $^{131}$I followed by both a WBS SPECT scan, and planar head and neck scan, two days later. If no evidence of thyroid remnant is found, the treatment is over, but the patients should be followed up 12 months later.

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**Study Population**

- 60 patients (60) who had undergone thyroidectomy, had no confirmed metastases (TxN0M0 stage), and who had been declared cured at the Tran Hung Dao Hospital, Hanoi, April - June 2015, were included.
  - Declared cured, meant that autoantibody Thyroglobulin (TgAb) level was in the normal range (0-4.8 µg/ml) and that neither the ultrasound nor the radiography detected any remaining thyroid images.
  - The levels of the protein Tg should also be below 1 ng/ml in the blood, if the patient get thyroid hormone, and less than 2 ng/ml if the patient does not get thyroid hormone.

The measurements were performed when the patients visited the hospital for a second follow up examination, 6-8 months after their treatments, to certify that there were no thyroid cancer cells left.
Primary Indications and Preparations

- **Primary Indications:** Measurement of the thyroidal uptake of radioactive iodine (131I) was performed together with measurements of the Thyroid Stimulating Hormone (TSH) in the blood to diagnose if the thyroid cancer is cured or not.

- **Dosage:** 5 mCi 131I as sodium iodide solution

- **Route of Administration:** Oral

- **Patient Preparation:** Treatment with propylthiouracil or methimazole should be discontinued at least 3 days before measurement of the thyroid uptake.

- **Patient Positioning:** Sitting erect

- **Acquisition time:** 5 minutes

- **Administration Process:** Before dispensing of 131I, it should be reconfirmed that the patient has not received interfering medications (e.g., antithyroid drugs, thyroid hormone, and contrast agents) or other radio-pharmaceuticals (especially previous administration of 131I).

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Measurements

- The measurements of the thyroid 131I activity uptake in the anterior neck, thigh and phantom were performed with an Australrad mini Fukushima detector 2 days after administration of the 131I.

- The detector system was a standard Model Le Torch, which consists of a NaI (Tl) detector with an attached photo multiplier tube (PMT).

- The uptake was always measured at a distance of 25 cm between the face of the detector crystal and the anterior neck.

- Measurements of the 131I activity were also performed for a neck phantom containing one 131I standard solution vial (5 mCi) and of the patient’s thigh for estimation of the natural radiation in the patient’s body.
After the measurements, the patient’s thyroid $^{131}$I uptake was calculated according to:

$$RAIU(\%) = \frac{\text{neck/s counters (cpm)} - \text{thigh/s counters (cpm)}}{\text{Admi.activity counters (cpm)} - \text{background’s counters (cpm)}} \times 100$$

Where: $RAIU$ is the $^{131}$I uptake in the patient; $Admi.activity$ counters is a neck phantom containing one $^{131}$I standard solution vial (5 mCi).

In addition to the $RAIU$ measurements, Tg levels in the blood of the patients were measured.

The patients were also measured with single photon emission computed tomography SPECT, and the results for the patients who were declared stable or cured after these examinations were listed in one group (1) and the patients who were not declared cured were are listed in another group (2).
**Results**

<table>
<thead>
<tr>
<th>Group:</th>
<th>1 (cured)</th>
<th>2 (not cured)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patients:</td>
<td>40</td>
<td>20</td>
</tr>
<tr>
<td>Mean value of RAIU:</td>
<td>0.24</td>
<td>3.45</td>
</tr>
<tr>
<td>SD of RAIU:</td>
<td>0.30</td>
<td>1.71</td>
</tr>
<tr>
<td>SEM-RAIU:</td>
<td>0.048</td>
<td>0.39</td>
</tr>
</tbody>
</table>

SD: Standard Deviation: \( SD = \sqrt{\frac{\sum (x - \mu)^2}{N}} \)

SEM: The standard error of the mean value: \( \sigma_x = \frac{\sigma}{\sqrt{n}} \)

*These results agreed well with the protein Tg level in the blood of the patients and the SPECT results!*

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**Discussion and Conclusion**

- We show a simple and relatively low cost method which can be used at local nuclear medicine departments/medical centers outside of the major cities to follow thyroid cancer patients who have had their thyroid surgically removed (thyroidectomy), without any metastases, and have been declared cured.

- The method is based on using a small NaI (Tl) detector system and oral intake of \(^{131}\text{I}\), to measure the concentrated radioactive iodine uptake (RAIU), together with protein Tg level in the blood of the patients.
Discussion and Conclusion

- We showed that the mean value of RAIU for the patients who were declared stable or cured based on the SPECT and Tg measurements was 0.24.

- The mean value of RAIU for the patients who were declared not cured was 3.45, so it can be seen that there is significant difference in the RAIU values for the stable/cured and not cured patients.

- These results are fully consistent with earlier published results, e.g. [1].


Possible Future Development

- The detector system should be fixed with a fixed patient position to certify that there is always the same distance between the detector’s crystal and the patient’s anterior neck, thigh, as well as the phantom.

- The detector system should include lead shielding to reduce background counts, and should be collimated to reduce scattering and to enhance counting statistics.

- There should be options of pre-set measuring times.
Further research is also recommended to compare the costs of establishing and maintaining nuclear medicine facilities outside of the major cities with the cost of transporting patients to a fully equipped hospital.

For more detailed information, please see:

A review of thyroid cancer and follow up screening after initial treatment

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Thank you very much for your attention!!