

# International Czech and Slovak cooperation in the treatment of patients with differentiated thyroid cancer

Otakar Kraft<sup>1</sup>, Ivan Režňák<sup>2</sup>

<sup>1</sup>Department of Nuclear Medicine, University Hospital, Ostrava-Poruba, Czech Republic

<sup>2</sup>Department of Nuclear Medicine, University Hospital, Martin, Slovak Republic

[Received 23 III 2006; Accepted 7 VI 2006]

## Abstract

**BACKGROUND:** The aim of this paper is to present our experience concerning cooperation in the treatment of Slovak patients with differentiated thyroid cancer in Slovak and Czech hospitals. The objectives of this study were to demonstrate the means of this cooperation and the results of therapy.

**MATERIAL AND METHODS:** From September 1991 to October 2005 in the Department of Nuclear Medicine in Ostrava 357 patients from the Slovak Republic with differentiated thyroid cancers (follicular and papillary) underwent complex therapy. They were diagnosed and operated due to the cancer (near-total thyroidectomy and removal of lymph node metastases) in Slovak hospitals. Then they were sent to the Department of Nuclear Medicine in Ostrava in the Czech Republic. In this department a radioiodine ablation of thyroid remnants, by means of the treatment amount of radioiodine of a standard activity of 3.7 GBq, was performed, and then a suppression and substitution therapy of thyroid hormones was started. After 3–6 months some patients were examined by means of diagnostic whole body scintigraphy after application of 300 MBq <sup>131</sup>I. Some patients were treated by means of a standard activity of 7.4 GBq <sup>131</sup>I and after 5 days whole body scintigraphy (WBS) was performed.

In both of these groups of patients the diagnostic or therapeutic radioiodine application was done after withdrawal of thyroid hormone treatment. If thyroglobulin levels were low and WBSs were negative, patients were followed up in the Department of Nuclear Medicine in Martin. Patients with radioiodine accumulated metastases were again treated with radioiodine in Ostrava. If indicated, external radiation therapy targeted on the neck and upper mediastinum was performed in the Slovak Republic, in the University Hospital in Martin. Newly formed lymph node metastases were surgically treated in Slovakia, too. Generally we have very good treatment results. Also, economically our partnership is cost effective. Our collaboration also successfully continues after entrance of the Slovak Republic and the Czech Republic to the European Union in 2004.

**CONCLUSIONS:** The results of this multi-centre study show that international Czech and Slovak cooperation in the complex therapy of patients with differentiated thyroid cancers is successful, with high efficacy. The treatment results were very similar to therapeutic results in our patients from the Czech Republic.

**Key words:** thyroid differentiated cancer, thyroidectomy, radioiodine therapy, thyroid cancer, thyroid radioiodine accumulation

## Introduction

We present our experience concerning cooperation in the treatment of Slovak patients with differentiated thyroid cancers (DTC) in Slovak and Czech hospitals. Treatment capacities in Slovak nuclear medicine departments are not sufficient for radioiodine therapy and that is why these patients are sent for this therapy to the Czech Republic nuclear medicine departments. The objectives of this study are to demonstrate the means of this cooperation and the results of the therapy. We concentrated on the collaboration between the Department of Nuclear Medicine in Martin in the Slovak Republic and the Department of Nuclear Medicine in Ostrava in the Czech Republic.

Until 1991, patients with DTC were treated in Slovak hospitals in two departments of nuclear medicine — in Bratislava and Martin. In 1991, in the department of nuclear medicine in Martin,

Correspondence to: Otakar Kraft  
Department of Nuclear Medicine, University Hospital  
17. Listopadu 1790, 708 52 Ostrava-Poruba, Czech Republic  
Tel: (+42) 597 372 290, fax: (+42) 596 919 156  
e-mail: otakar.kraft@fnspo.cz

a malfunction in the waste water liquidation system after radioiodine therapy occurred. From this time patients with DTC could only be followed up in Martin hospital and because of the small number of nuclear medicine beds in Slovak hospitals these patients had to be treated by means of radioiodine application abroad (in the Czech hospitals).

In our paper we present our knowledge on international cooperation in the treatment of 357 patients from Slovakia who were treated in the Department of Nuclear Medicine of the University Hospital in Ostrava in the Czech Republic from September 1991 to October 2005.

## Material and methods

### Patients and procedure

From September 1991 to October 2005 357 patients from the Slovak Republic with DTC underwent complex therapy. In Slovak hospitals they were diagnosed and operated due to thyroid cancer (near-total thyroidectomy and removal of lymph node metastases). Then they were sent to the Department of Nuclear Medicine in Ostrava, Czech Republic.

In this department a radioiodine ablation of thyroid remnants by means of the treatment standard activity of 3.7 GBq radioiodine was performed and then a suppression and substitution therapy of thyroid hormones was initiated. After 3–6 months 244 patients were examined by means of diagnostic whole body scintigraphy after application of 300 MBq  $^{131}\text{I}$  utilizing a dual-head SPECT gamma-camera E.CAM (Siemens, Erlangen, Germany) equipped with high energy collimators; the scanning was performed 48 hours after radioiodine application (Fig. 1A, 2). In 243 patients diagnostic whole body scintigraphy (WBS) was negative. One patient with accumulated metastasis did not arrive, and the therapy was not done.

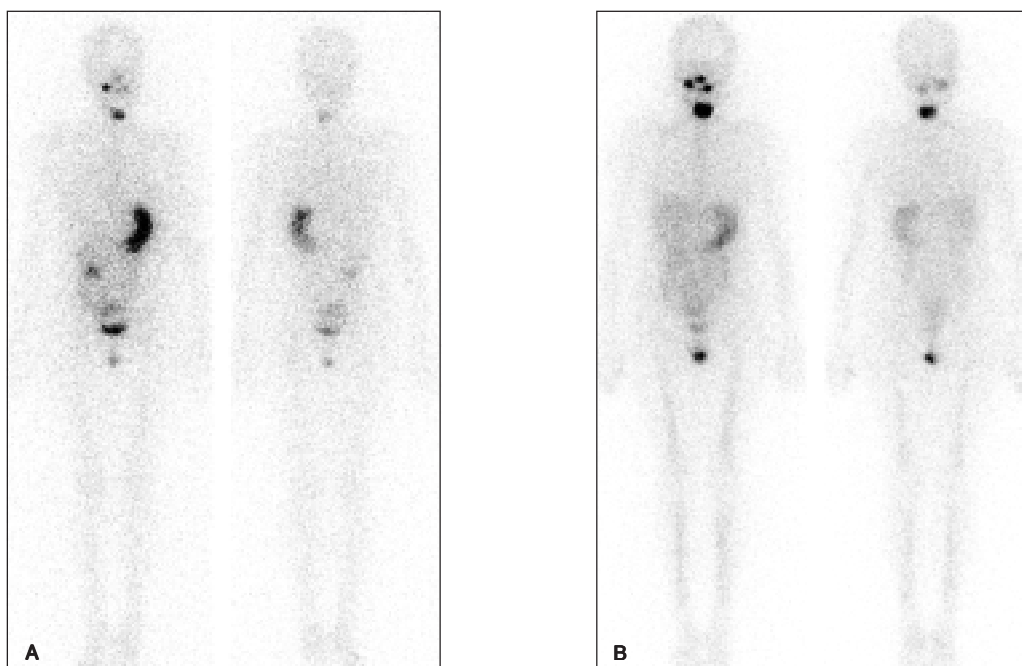
The rest of the patients (113 patients) with accumulated metastases or radioiodine accumulated thyroid remnant were treated by means of standard activity of 7.4 GBq  $^{131}\text{I}$  (2–5 months after radioiodine thyroid ablation) and post-therapeutic WBS was performed after 5 days (Fig. 1B, 3–5). In both these groups of patients the diagnostic or therapeutic radioiodine application was done after withdrawal from thyroid hormone treatment. Thyroid stimulating hormone (TSH), free thyroxin (FT4), total triiodothyronin (TT3), thyroglobulin (Tg) and antithyroglobulin antibodies (TgAb) were tested in plasma from all patients. From September 1991 to October 2005 we treated 357 Slovak patients (70 men and 287 women, average age 48.4 years) in Ostrava with radioiodine, in addition to Czech patients. 66 patients had follicular cancers and 291 papillary cancers (included 77 patients with follicular variants of papillary cancer).

## Results

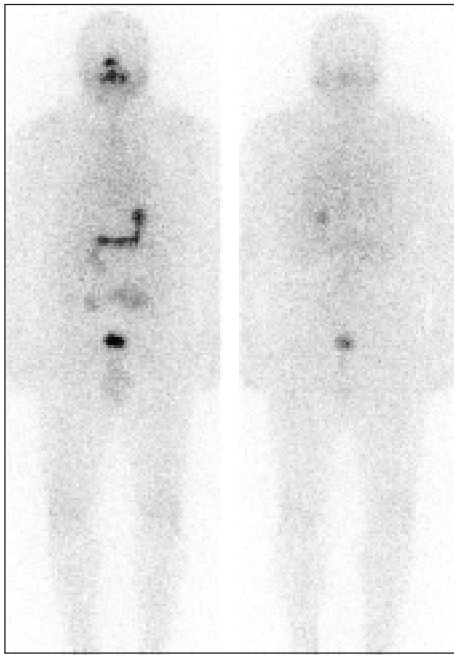
From a total of 357 patients 231 had one thyroidectomy, 106 pts had two surgeries and 20 patients had three thyroidectomies (Table 1).

Eighty-seven patients (24.4%) had radioiodine accumulating metastases: 78 patients (21.8%) in lymph nodes, 2 patients (0.56%) in lymph nodes and bones, 3 patients (0.84%) in lymph nodes, lung and bone, one patient (0.28%) in lymph node and liver, one patient (0.28%) in lymph node, lung and liver and two pts (0.56%) in bones (Table 2).

After thyro-elimination, diagnostic whole body scintigraphy without radioiodine therapy was done in 244 patients — WBS in 243 patients was negative; in one patient accumulated lymph node metastasis was found. Following therapy was not performed, as the patient did not arrive.



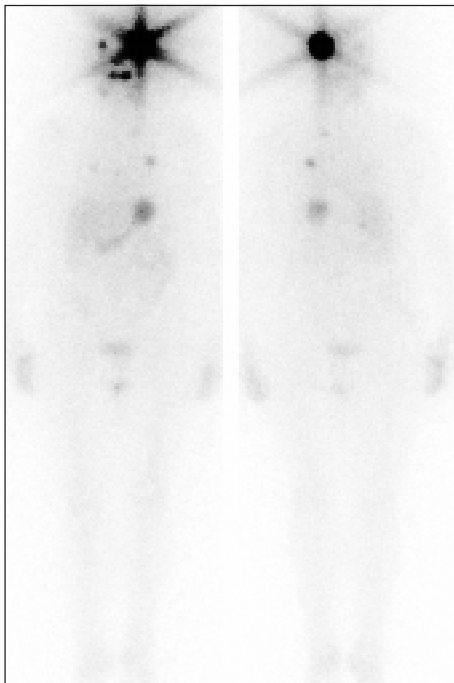
**Figure 1.** Woman aged 42 years with papillary thyroid cancer after thyroelimination. **A.** Diagnostic whole body scintigraphy; **B.** Post-therapeutic whole body scintigraphy — markedly accumulated thyroid remnant.



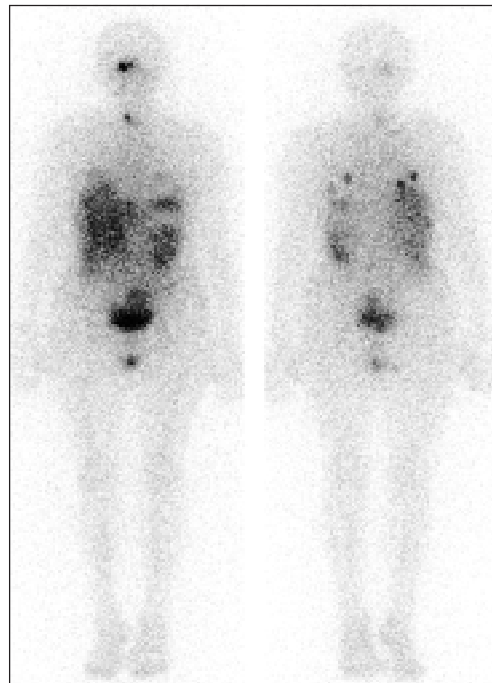
**Figure 2.** A 43 year-old man with papillary thyroid cancer. Diagnostic scintigraphy after 300 MBq of  $^{131}\text{I}$ . Without thyroid remnant or accumulated metastases.



**Figure 3.** Woman aged 65 years. Repeated radioiodine therapy for pulmonary metastasis of follicular thyroid cancer. Scintigraphy after therapy 7.4 GBq  $^{131}\text{I}$ .



**Figure 4.** Woman aged 55 years with papillary thyroid cancer. Scintigraphy after therapy 7.4 GBq  $^{131}\text{I}$ . Thyroid remnant and accumulated pulmonary metastases.



**Figure 5.** Woman aged 64 years with follicular thyroid cancer. Scintigraphy after therapy 7.4 GBq  $^{131}\text{I}$ . Accumulated pulmonary and bone metastases.

**Table 1. Number of one, two or three thyroidectomies**

THYROIDECTOMY	
One surgery	231
Two surgeries	106
Three surgeries	20
Total	357

### Radioiodine therapy

Single  $^{131}\text{I}$  therapy was done in 68 patients — post-therapeutic or diagnostic whole body scintigrams were negative in 67 patients, one patient had pulmonary metastasis. After two radioiodine therapies in 6 patients from 22 patients there were lymph node or pulmonary metastases or a combination of lymph node, pulmonary and liver metastases. The other 16 patients had negative

**Table 2. Number of various types of accumulated metastases**

RADIOIODINE ACCUMULATED METASTASES	
In lymph nodes	78
In lymph nodes and bones	2
In lymph nodes, lung and bone	3
In lymph node and liver	1
In lymph node, lung and liver	1
In bones	2
Total	87

post-therapeutic WBS. After three therapies two patients had metastases in bones or lung. After four therapies in one patient (only one received four therapies) we found thyroid remnants. After 5 therapies in 4 patients from the eight, lymph nodal or pulmonary metastases were shown, and the other 4 patients were without accumulated metastases. One patient was treated six times. After the sixth radioiodine therapy this patient showed pulmonary metastasis. One patient was treated 7 times for liver metastasis. All 4 patients, after eight and nine therapies, had negative whole body scans. One patient, after 12 therapies, showed lymph node metastasis (Table 3).

All patients with metastases shown after these therapies will be treated by radioiodine again in Ostrava, Czech Republic.

## Discussion

Thyroid carcinoma accounts for approximately 1% of all human cancers. The most often there are DTCs, which are divided according to histopathological classification into follicular and papillary carcinomas.

DTC often forms metastases in lymph nodes on the neck, distant metastases in lungs and bones. Other distant metastases — to the brain, kidneys, skin and liver [1] are rare.

Radioiodine therapy is used in patients with DTC for ablation of thyroid remnants and for treatment of persistent or recurrent disease. Its use depends upon the ability of neoplastic cells to concentrate radioiodine.

Favourable responses to treatment are characterised by parallel decreases in tumour volume,  $^{131}\text{I}$  uptake and serum Tg levels. In contrast, a decrease in  $^{131}\text{I}$  uptake without a parallel decrease, or with an increase in tumour volume, indicates tumour progression. The overall survival rate at 10 years from the time of detection of metastases ranges from 25–40%. Distant metastases appear to be the main cause of thyroid cancer-specific mortality, but are compatible with long-term survival in numerous patients [2–4]. Prognostic variables for survival are strongly interrelated, and multivariate analyses have shown that four variables have a favourable impact: young age at the time of metastases detection, the papillary or follicular histological type of the primary tumour, the presence of  $^{131}\text{I}$  uptake, and small extent of the disease. The survival rate at 10 years was 93% in patients who achieved a complete response but only 14% in those who did not [2]. This finding does not signify that prolonged survival can be imputed to therapy alone, since response to treatment was also related to other favourable prognostic factors. All patients who survived 15 years or more after the discovery of the metastases, however, had been treated with  $^{131}\text{I}$ . Without radioiodine therapy, it is very unlikely that such a large number of patients would be alive for such a long period of time after the discovery of metastases [2].

For follow-up of patients with DTC, after the elimination of the thyroid gland, the regular determination of serum levels of thyroglobulin is important; this is a sensitive and specific tumour marker. In a small number of cases it can be false negative. The thyroglobulin assessment is periodically supplemented by whole body scintigraphy after a diagnostic amount of radioiodine, after withdrawal of thyroid hormone treatment. The possibly present functional metastases are stimulated by subsequent increased level of TSH. Whole body scintigraphy is false negative in non-functional metastases. In this situation the determination of serum thyroglobulin helps [5].

In diagnosis, therapy and long-term follow up of patients we use procedures which are ordinarily recommended and used in the therapy of DTC throughout the world [6–11].

In preparation of patients for radioiodine therapy we did not use Thyrogen, recombinant human TSH (rhTSH) [12], especially for economic reasons (Thyrogen is not reimbursed by our health insurance system).

**Table 3. Number of  $^{131}\text{I}$  treatments and whole body scans in our patients with metastases or radioiodine-accumulating thyroid remnants**

$^{131}\text{I}$ therapy 7.4 GBq	Number of patients	Post-therapeutic or diagnostic WBS		
		Negative	Positive	Localization of metastasis
1 <sup>st</sup>	68	67	1	Lung
2 <sup>nd</sup>	22	16	6	Lymph node, lung, liver
3 <sup>rd</sup>	2		2	Bone, lung
4 <sup>th</sup>	1		1	Thyroid remnant
5 <sup>th</sup>	8	4	4	Lymph node, lung
6 <sup>th</sup>	1		1	Lung
7 <sup>th</sup>	1		1	Liver
8 <sup>th</sup>	4	4		
9 <sup>th</sup>	4	4		
12 <sup>th</sup>	1		1	Lymph node
Total	113	96 (85%)	17 (15%)	

## Conclusions

In conclusion we generally had very good treatment results in patients from Slovakia which did not differ from the results achieved in patients from the Czech Republic.

Due to this, some facts should be remembered. We took these facts into consideration during the treatment of Slovak patients which for us are, today, patients from abroad. Until the end of 1992 Czech and Slovak people lived in one state — Czechoslovakia, which subsequently was divided into two states — the Czech and the Slovak Republics. During the delivery of information which was necessary for successful therapy generally there were no problems in communication with patients due to the similarity of the Slovak and Czech languages. After thirteen years of division of the Czechoslovak Republic principles of health care maintenance did not substantially differ. Also, their similar lifestyles and living standards did not significantly change. Some differences in the reform of health care and health insurance induced predominantly administrative drawbacks in therapeutic supply. In about 10% of patients the thyroablative radioiodine amount was not given in the optimal interval of 6 weeks after thyroidectomy but after a further two to four weeks.

Our partnership is also effective economically. Our collaboration has successfully continued after the entrance of the Slovak Republic and the Czech Republic to the European Union in 2004. The results of this multi-centre study show that international Czech and Slovak cooperation in the complex therapy of patients with differentiated thyroid cancers is successful, with high efficacy. The treatment results were very similar to therapeutic results in our patients from the Czech Republic.

The interest of our presentation lies on the following:

- by the WBS we found no metastases in the kidneys, brain or the skin [1];
- in accordance with our experience, a favourable response to treatment was characterised by a parallel decrease of the tumour volume, <sup>131</sup>I uptake and serum Tg levels [13];
- while preparing patients for radioiodine therapy we did not use recombinant human TSH for administrative and financial reasons [12];
- after one to twelve radioiodine therapies the WBS in 85 percent of patients was negative with normalization of Tg levels indicating successful <sup>131</sup>I therapy [14];
- patients may take up to 66.6–88.8 GBq of <sup>131</sup>I within a 10 year period [15].

This is a randomised study. Selected patients will be studied and presented on forthcoming occasions.

This paper was presented as an oral presentation in WFNMB/WRPTC International Conference on Radiopharmaceutical Therapy (ICRT-2005), Limassol, Cyprus 11–14 October 2005 [16].

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