

Bone metastases of differentiated thyroid cancer: impact of early ^{131}I -based detection on outcome

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Abstract

Bone is the second most frequent target of distant metastases in patients with differentiated thyroid cancer, and such forms carry a very poor prognosis. The impact of ^{131}I therapy in this setting is controversial. We describe the diagnostic circumstances and outcome of patients with bone metastases recently managed in two institutions. Among 921 consecutive thyroid cancer patients who had total thyroidectomy and ^{131}I ablation between January 2000 and December 2004 and who were subsequently monitored, bone metastases had been diagnosed in 16 patients. In three cases, the bone metastases were non-functioning (negative ^{131}I uptake). These patients were treated with surgery and radiotherapy but progressed rapidly. The other 13 patients had functioning (positive ^{131}I uptake) bone metastases. In five of them, thyroid cancer was revealed by signs of distant involvement (bone pain, $n=4$; dyspnea, $n=1$). The bone metastases progressed in these five patients, despite local therapy and multiple courses of ^{131}I . The bone metastases in the remaining eight patients were discovered on the post-surgery ^{131}I therapy scan. Complementary radiological studies were negative except in one patient in whom one of the metastases (a 5 mm lesion of the right humerus) was visible on magnetic resonance imaging (MRI). Six of these patients showed a good response to ^{131}I therapy, with ^{131}I uptake and Tg levels becoming undetectable or showing a sharp fall. One patient refused ^{131}I therapy; bone metastases became visible on MRI within 1 year and the Tg level rose tenfold. The disease progressed in one patient despite ^{131}I therapy. Post-surgical ^{131}I ablation can contribute to early detection of bone metastases at a time when the Tg level may be only moderately elevated, when other radiological studies are negative, and when the disease is potentially curable by ^{131}I therapy.

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Introduction

About 3 to 5% of patients with differentiated thyroid cancer develop bone metastases (Bernier *et al.* 2001, Haq & Harmer 2005, Durante *et al.* 2006). Bone metastases are less frequent than pulmonary metastases but carry a far worse prognosis (Haq & Harmer 2005, Durante *et al.* 2006).

Iodine 131 (^{131}I) has been used since 1946 to treat patients with functioning metastases (Seidlin *et al.* 1946). ^{131}I uptake is found in more than two-thirds of patients with distant metastases and in roughly equal proportions of patients with lung or bone involvement (Duranter *et al.* 2006). However, the impact of ^{131}I therapy on bone metastases is controversial (Proye *et al.* 1992).

In a historical report by Brown, only 1 (5%) out of 21 patients with bone metastases treated with ¹³¹I survived 5 years (Brown *et al.* 1984), but efficacy seems to have improved in recent years (Bernier *et al.* 2001, Petrich *et al.* 2001, Haq & Harmer 2005, Durante *et al.* 2006). Bernier *et al.* (2001) obtained a 15% survival rate at 10 years in patients with bone metastases. By comparison, more than 60% of patients with metastases confined to the lungs survive for 10 years (Casara *et al.* 1993, Hindié *et al.* 2003, Durante *et al.* 2006).

Bone metastases are rarely detected at an early stage. Here, we analyzed the diagnostic circumstances and outcome of patients with bone metastases in a series of patients with differentiated thyroid cancer recently managed in two institutions.

Patients and methods

From January 2000 to December 2004, a total of 921 patients with newly diagnosed differentiated thyroid cancer received total thyroidectomy and ablation therapy with 100 mCi (3.7 GBq) ¹³¹I, either at the Nuclear Medicine Department of Saint-Antoine Hospital or at Saint-Louis Hospital (Paris, France), and were subsequently monitored. The first follow-up examination, 6–12 months after ablation therapy, included Tg assay under thyroid-stimulating hormone stimulation.

This analysis focuses on 16 patients (11 females and 5 males) in whom bone metastases were discovered either during the initial work-up or during follow-up. Their mean age was 57.2 years (16–77 years). No other case of bone metastases occurred during the follow-up period of this study (average 45 months).

Non-functioning metastases

Three patients had bone metastases that were non-functioning, i.e., did not take up ¹³¹I. These three patients were treated with surgery and/or external beam radiotherapy (Table 1).

Functioning metastases

In the other 13 patients, all the bone metastases were functioning (¹³¹I-avid). Four of these patients also had functioning lung metastases (Table 2). When bone metastases were suspected on the basis of ¹³¹I whole-body scan, and in order to precisely locate ¹³¹I foci, ¹³¹I scanning was repeated and combined with ^{99m}Tc-HMDP (^{99m}Tc-hydroxy-methylene-diphosphonate) bone scanning, using simultaneous dual-tracer planar imaging, and SPECT (single photon emission computerized tomography) imaging if necessary. In both the institutions, scanning was done with a double-head gamma camera (DST-XL,

GEMS). Radiological studies were also performed in every case.

Patients with functioning metastases received repeated courses of ¹³¹I, consisting of 100 or 150 mCi every 6 months until uptake was no longer detected on the therapy scan. Repeat therapy was not preceded by diagnostic scanning. Additional therapy (surgery and/or external beam radiotherapy) was given in six cases (Table 2).

Before any ¹³¹I therapy, patients were instructed to avoid food and medication with high iodine content (a specific list is given). Moreover, urinary iodine was measured in all patients. All patients were thoroughly informed of ¹³¹I therapy and imaging studies.

This retrospective study was done in compliance with the ethical requirements at our Institution.

Results

Discovery of non-functioning metastases

In two patients (patients B and C), bone pain was the first symptom of thyroid cancer. In the third (patient A), non-functioning metastases of the cervical spine were discovered, together with neck soft tissue recurrence, 12 months after initial management, and were documented by FDG PET-CT (fluorine-18-deoxyglucose positron emission tomography/computerised tomography) and MRI (Table 1).

Outcome of patients with non-functioning metastases

The three patients concerned had a rapidly progressive disease, despite various treatments (Table 1), and survived for 5 to 34 months (mean 19.3 months; Table 1).

Discovery of functioning metastases

Thyroid cancer was revealed by signs linked to distant metastases in five cases. Back pain was the first symptom of thyroid cancer in four patients (nos 2, 6, 8, 11) and was associated with spinal cord compression in three cases. Dyspnea was the revealing symptom in one patient (no. 13); computerised tomography (CT) showed the presence of multiple lung and bone metastases and an enlarged thyroid. The distribution of bone metastases at initial ¹³¹I therapy in these five patients is shown in Table 2. Off-T4 Tg levels ranged between 31 and 86 960 ng/ml (Table 2).

In the other eight patients, bone metastases were revealed by ¹³¹I scanning during ¹³¹I remnant ablation in seven cases (nos 1, 3, 4, 5, 7, 9, 12), and, in the last case (patient no. 10), during a second course of ¹³¹I given because of a high initial Tg level (147 ng/ml) and because

Table 1 Patients with non-functioning bone metastases (no ^{131}I uptake)

Patient number	Sex	Age ^a	Histology	Tumor and node stage	Tg (ng/ml) off-L-T ₄	Data at diagnosis of bone metastases			Treatments			Patient state
						Mode of discovery	Initial distant sites of ^{131}I uptake	Radiological studies	Cumulated ^{131}I activity (mCi)	Other treatments	Follow-up ^b	
A	F	65	Papillary	T4bN1b	1955	Local recurrence at 1 year	Non-functioning	MRI, CT and PET: tumor extension to C6	300	Spine radiotherapy	34 months	Deceased
B	M	66	Follicular, insular areas	T3N1b	12	Bone pain	Non-functioning	X-ray: right femur MRI: L2 and L5	300	Femur: surgery + radiotherapy	19 months	Deceased
C	M	73	Hürthle	T3N1b	52	Bone pain	Non-functioning spine metastases. One functioning metastasis in skull	MRI: multiple spine metastases	100	Cervical spine radiotherapy	5 months	Deceased

^aPatient age (in years) at thyroid surgery (patients are classified according to age at diagnosis).

^bFollow-up in months from diagnosis of bone metastases.

of the large size of the initial thyroid tumor (7 cm). The distribution of bone metastases at initial ^{131}I therapy in these eight patients is shown in Table 2. The off-T₄ Tg level at diagnosis of bone metastases ranged between 7.4 and 9020 ng/ml. In four cases, the stimulated Tg level was lower than 40 ng/ml (nos 3, 4, 5, 7). Complementary radiological studies were negative in seven patients. In the remaining one patient (no. 1), MRI showed a single metastasis (a 5 mm lesion of the right humerus).

Outcome of patients with functioning metastases

The five patients in whom thyroid cancer was revealed by distant metastases (patient nos 2, 6, 8, 11, 13) had a mean follow-up of 49 months. Two of them (nos 6, 8) died. Patient no. 6 received treatment with an anti-angiogenic drug (Nexavar Sorafenib, Bayer), during the last 3 months, which gave a temporary improvement of dyspnea, together with a transient reduction of the size of pulmonary nodules and Tg levels. Two others patients (nos 11, 13) have progressive disease despite multiple courses of ^{131}I and additional local treatments (Table 2). The fifth patient (no. 2) had a single (spinal) metastasis for which she received surgery, external beam radiotherapy, and a total of 524 mCi ^{131}I , but with an incomplete response (Table 2).

Among the eight patients (nos 1, 3, 4, 5, 7, 9, 10, 12) whose bone metastases were discovered by ^{131}I scanning, five are in an apparent remission after an average cumulative ^{131}I dose of 303 mCi and no additional therapy. ^{131}I uptake has disappeared in these five patients (Figs 1–3). Tg level has fallen markedly in two patients (from 511 to 1.7 ng/ml in patient no. 1 (Fig. 1) and from 22 to 4 ng/ml in patient no. 5 (Fig. 2)), and is undetectable in the other three patients (nos 3, 4, and 7 (Fig. 3)). Another patient (no. 12) had an excellent response and is continuing ^{131}I therapy. She has a slight residual ^{131}I uptake at a single site, while the other bone and lung ^{131}I foci have disappeared, and the off-T₄ Tg level has fallen from 194 to 10.9 ng/ml. One of the other two patients (patient no. 9) has a progressive disease with new bone metastases despite ^{131}I therapy and local treatments, and died 63 months after the discovery of bone metastases. The other patient (no. 10), who had focal ^{131}I uptake in the left femur, refused additional therapy because MRI showed a normal femur. She finally accepted therapy 18 months later because of a rise in Tg levels on L-T₄ therapy. At this time, the ^{131}I scan showed multiple bone metastases which were also clearly visible on MRI, and the off-T₄ Tg level which had increased from 180 to 2234 ng/ml. Disease is now progressing despite ^{131}I therapy.

Table 2 Patients with functioning (^{131}I avid) bone metastases

Patient number	Sex	Age ^a	Histology	Tumor and node stage	Data at diagnosis of bone metastases				Management			Data from the last ^{131}I therapy (off-LT ₄)			Patient state
					Tg (ng/ml) off-LT ₄	Mode of discovery	Initial distant sites of ^{131}I uptake	Radiological studies	Cumulated ^{131}I activity (mCi)	Other treatments	Follow-up ^b	Residual ^{131}I uptake	Tg (ng/ml)	Last Tg (under rhTSH)	
1	F	16	Papillary	T2N1b	519	^{131}I Post-surgery	<i>R. humerus, occipital, L. acetabulum</i> +lung	MRI: positive only for humerus (5 mm lesion)	516	No	86 months	No	11.5	1.7	Apparent remission (detectable Tg)
2	F	27	Follicular (Hurthle areas)	T2Nx	206	Pain; medullary compression	Spine (T2)	Spine MRI: positive	411	Spine: surgery + radiotherapy	43 months	T2	133		Partial response
3	F	34	Papillary	T3Nx	28	^{131}I Post-surgery	Spine L4, <i>R. sacroiliac</i>	MRI: negative. Bone scan: negative	200	No	8 months ^c	No	<1		Apparent remission
4	F	45	Papillary	T1N1b	18	^{131}I Post-surgery	Left 7th rib	CT: negative, bone scan: negative	100	No	54 months	No ^d	<1	<1	Apparent remission
5	M	48	Papillary	T1Nx	22	^{131}I Post-surgery	Spine T6 and L2, <i>R. scapula, L. iliac</i>	MRI: negative, bone scan: negative	450	No	37 months	No	4		Apparent remission (detectable Tg)
6	M	53	Follicular (poorly differentiated)	T4aN1b	31 (positive TgAb)	Bone pain	Spine T6, left 7th rib, pelvis	MRI: positive, bone scan: positive	524	Spine: surgery + radiotherapy pelvis: surgery	76 months	Multiple new bone and lung metastases	149 (positive TgAb)		Deceased
7	M	55	Papillary (Hurthle areas)	T1Nx	7.4	^{131}I Post-surgery	Spine: T11, L3	MRI: negative, bone scan: negative	250	No	23 months	No	<1	<1	Apparent remission
8	F	63	Follicular	T2Nx	12 888	Pain; medullary compression	Spine: T10 and T11, sternum, <i>R. iliac</i>	MRI: T9, T10, T11 (compression), L1, L4	750	Spine and skull radiotherapy	32 months	Skull, spine, sternum, iliac	74 640		Deceased
9	F	67	Papillary	T4aN1b	9020	^{131}I Post-surgery	Right 10th rib and manubrium	MRI: negative, bone scan: negative	413	^e L humerus: Surgery + radiotherapy	63 months	<i>L Humerus</i> , Retro-sternal uptake	2810		Deceased

Table 2 continued

Patient number	Sex	Age ^a	Histology	Tumor and node stage	Data at diagnosis of bone metastases				Management			Data from the last ¹³¹ I therapy (off-LT ₄)		Patient state
					Tg (ng/ml) off-LT ₄	Mode of discovery	Initial distant sites of ¹³¹ I uptake	Radiological studies	Cumulated ¹³¹ I activity (mCi)	Other treatments	Follow-up ^b	Residual ¹³¹ I uptake	Tg (ng/ml)	
10	F	74	Papillary	T3Nx	180	2nd ablative ¹³¹ I Post-surgery ^f	Left femur (residual bed uptake)	MRI: negative, PET: negative, bone scan: negative	550	No	29 months	<i>L femur</i> ; R 4th rib; skull	4926	Progressive disease
11	F	75	Follicular	T3N0	86 960	Pain; medullary compression	T12, <i>L iliac</i> , sternum + Lung multiple	CT: T12 (compression) + Lung multiple, bone scan: positive	1150	T12: surgery + radiotherapy, pelvis: surgery	62 months	Multiple bone and lung metastases	88 450	Progressive disease
12	F	77	Follicular	T2N0	194	¹³¹ I Post-surgery	Skull, sternum, ribs + lung multiple	CT thorax, skull: negative, bone scan: negative	550	No	63 months	Sternum	10.9	Partial response
13	F	77	Follicular (poorly differentiated)	T3N0	22 600 (positive TgAb)	Dyspnea; CT showed lung and bone metastases	Skull, ribs, <i>R. scapula</i> , <i>R. humerus</i> , <i>L. femur</i> + lung multiple	MRI: T12 (compression) CT: positive multiple PET: positive multiple	242	Spine: surgery + radiotherapy, skull: surgery	34 months	Lung, spine, ribs, <i>L. femur</i>	45 500	Progressive disease

^aPatient age (in years) at thyroid surgery. (Patients are classified according to age at diagnosis).

^bFollow-up in months from diagnosis of bone metastases.

^cThis patient could not have further stimulation tests because she left France.

^dPatient no. 4: the only case where disappearance of ¹³¹I uptake was documented on a diagnostic scan (5 mCi) and not on a therapy scan. (Because it was decided to give local therapy for the sole bone lesion in the case of persistent uptake or detectable Tg.) The patient had a second diagnostic scan 1 year later, which also was negative with stimulated Tg < 1 ng/ml. A rhTSH stimulation test 3 years later was also negative.

^ePatient no. 9: new bone metastases appeared during follow-up. She also had cementoplasty of T11.

^fAlthough the first post-surgery scan was negative, a second dose was given because of the elevated Tg level at first ablation dose (147 ng/ml), and tumor size (7 cm).

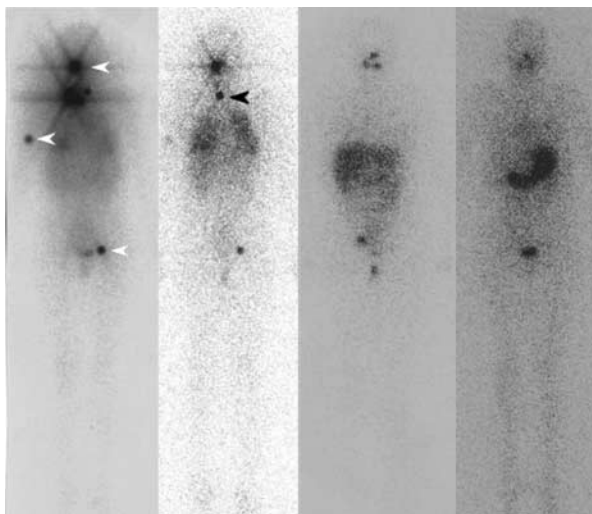


Figure 1 ^{131}I whole-body scans of patient no.1 (all scans are anterior views). The first scan (left) was obtained at the time of ^{131}I thyroid remnant ablation (100 mCi, off-T4 Tg 519 ng/ml). In addition to the uptake in the thyroid bed area, focal ^{131}I uptake is visible on the right humerus, the right occipital area, and the left acetabulum (arrowheads). There is also a faint pulmonary uptake. Complementary radiological studies were negative, except for the metastasis of the right humerus (5 mm on MRI). The second scan was recorded 5 months later during a second course of ^{131}I therapy (100 mCi, Tg=233 ng/ml). Some ^{131}I uptake is still visible on the right humerus, the right occipital area, and the left acetabulum. This scan also revealed an uptake on the manubrium (arrowhead), which was masked by the uptake in the thyroid bed during initial therapy. Diffuse lung uptake is now clearly visible. This third scan was obtained at 36 months, at the time of the fifth and last course of ^{131}I therapy (100 mCi, Tg=11.5 ng/ml). ^{131}I uptake at metastatic sites disappeared (the activity in the right pelvis corresponds to the bladder). The last scan was obtained with a diagnostic ^{131}I activity (5 mCi) after rhTSH stimulation, 18 months after the last course of ^{131}I therapy. No abnormal ^{131}I uptake was seen. Stimulated Tg=1.7 ng/ml.

Discussion

The poor prognosis associated with bone metastases of differentiated thyroid cancer (Brown *et al.* 1984, Niederle *et al.* 1986, Ruegger *et al.* 1988, Marcocci *et al.* 1989, Proye *et al.* 1992, Pacini *et al.* 1994, Schlumberger *et al.* 1996, Pittas *et al.* 2000, Van Tol *et al.* 2000, Bernier *et al.* 2001, Petrich *et al.* 2001, Zettinig *et al.* 2002, Eustatia-Rutten *et al.* 2003, Haq & Harmer 2005, Durante *et al.* 2006) might partly be due to the fact that they are rarely detected at an early stage. Among 109 patients with bone metastases described by Bernier *et al.* (2001), only 4 had both radioiodine uptake and a negative standard X-ray examination. Similarly, in the study by Durante *et al.* (2006), radiographs were negative at presentation in only 8 (7%) out of 115 patients. This series confirms the poor prognosis associated with bone macrometastases: no complete response was achieved in

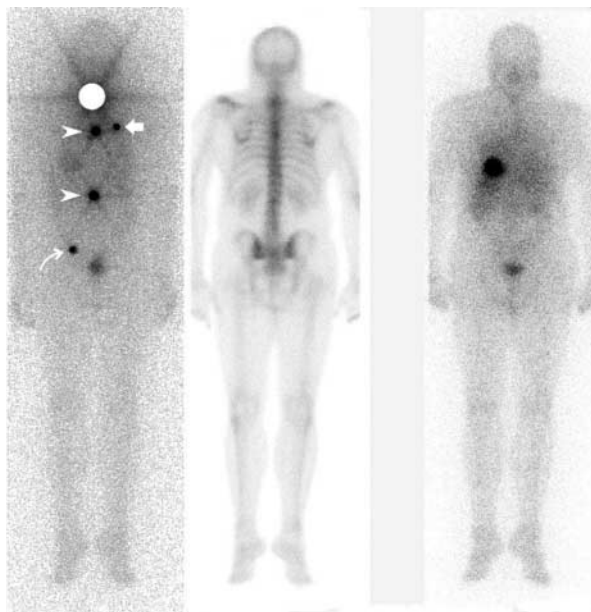


Figure 2 Whole-body scans of patient no. 5 (all scans are posterior views). The first scan (left) was obtained at the time of ^{131}I remnant ablation (100 mCi, off-T4 Tg=22 ng/ml). In addition to an uptake in the thyroid bed area (masked), focal ^{131}I uptake is visible on the spine at levels T6 and L2 (arrowheads), on the inner border of the right scapula (arrow), and on the left iliac bone (curved arrow). The precise location of the ^{131}I foci was possible by combining ^{131}I scanning with $^{99\text{m}}\text{Tc}$ -HMDP bone scanning (shown next to the ^{131}I scan), using simultaneous dual-tracer imaging. Bone scan *per se* is negative (the faint focus at level T6 is probably due to Compton scatter from ^{131}I in the technetium-99m window, as also seen at the level of the thyroid remnant). The ^{131}I scan on the right was obtained at 21 months, at the time of the third course of ^{131}I therapy (off-T4 Tg=4.2 ng/ml; TSH=50 $\mu\text{IU/ml}$). This scan shows the absence of residual ^{131}I uptake at metastatic sites (physiological uptake is seen corresponding to the stomach). A fourth course of ^{131}I therapy (3.7 GBq) was given 1 year later confirming the absence of residual ^{131}I uptake. The patient keeps a slightly elevated Tg level under stimulation (off-T4 Tg=4 ng/ml; TSH=59 $\mu\text{IU/ml}$).

such patients, even in case of positive ^{131}I uptake. The five patients with functioning macrometastases had a mean follow-up of 49 months. Despite intensive ^{131}I therapy and additional local treatments (Table 2), two patients died, two had progressive disease, and one had a partial response. The average survival time of three other patients with non-functioning metastases was much shorter (19.3 months). There are at least two explanations for a better outcome in patients with ^{131}I avid macrometastases, when compared with patients in whom bone metastases show no ^{131}I trapping: the first is that ^{131}I avidity probably implies a better differentiation of the tumor and the second is the impact of radiation delivered by ^{131}I . Intensive multimodality treatment is clearly justified in patients with functioning

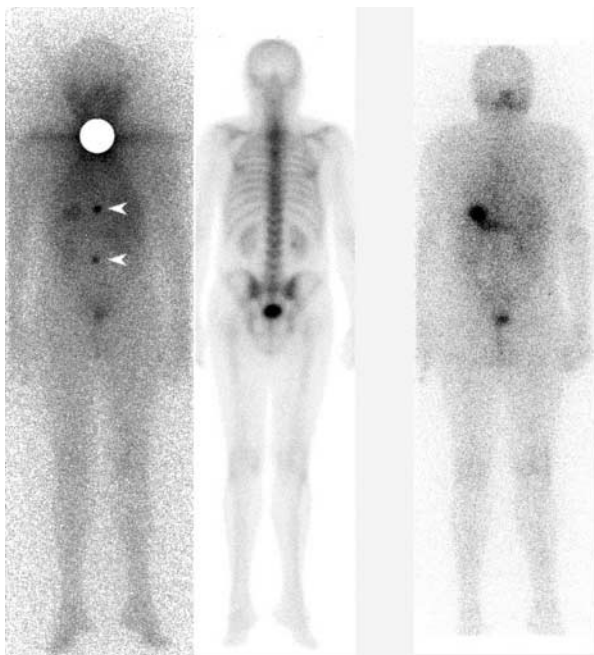


Figure 3 Whole-body scans of patient no. 7 (all scans are posterior views). The first scan (left) was obtained at the time of ^{131}I remnant ablation (100 mCi, off-T4 Tg=7.4 ng/ml). In addition to an uptake in the thyroid bed area (masked), two foci of ^{131}I uptake are visible on the spine at the level of T11 and L3 (arrowheads). The precise location of ^{131}I foci was obtained by combining ^{131}I scanning and $^{99\text{m}}\text{Tc}$ -HMDP bone scanning using simultaneous dual-tracer planar imaging and SPECT. The whole-body bone scan (shown next to the ^{131}I scan) is negative. The faint uptake in the upper thoracic spine is due to Compton scatter in the technetium-99m window from ^{131}I present in the thyroid remnant. The second ^{131}I scan was recorded 6 months later during the second course of ^{131}I therapy (150 mCi, off-T4 Tg ≤ 1 ng/ml). ^{131}I uptake at metastatic sites had disappeared (physiological uptake is seen in stomach and transverse colon).

macrometastases as it may allow for better survival. Whenever possible, FDG-PET should be obtained in patients with non-functioning metastases or those with functioning macrometastases. We believe that FDG-PET is an important complementary imaging study in these patients.

Our main finding is that a substantial percentage of bone metastases can now be discovered early on the ^{131}I scan, when tumor burden is still limited. A complete response to iodine therapy can be achieved at this early stage. In 8 out of the 16 cases in this series (50%), the bone metastases were first revealed by ^{131}I scanning. Complementary radiological studies were performed in all eight patients (MRI in six, CT in two, bone scan in seven). These imaging studies were negative in seven (cf. Table 2). In the remaining patient (patient no. 1), MRI showed a single metastasis. FDG-PET scan was not ordered on a routine basis in these patients (performed only in patient no. 10, in whom it

proved negative). A study by Ito *et al.* (2007) showed that the sensitivity of FDG-PET is similar to that of bone scanning, but with higher specificity.

At the time of ^{131}I ablation, the off-T4 Tg level in four patients with radiologically undetectable metastases was below 40 ng/ml, a value that some authors have proposed as a sign of possible distant metastasis (Schlumberger *et al.* 1996, Schlumberger 1998). In the absence of ablation therapy, early detection of bone metastases in these patients would not have been possible.

Several factors may have contributed to early detection of bone metastases, including trends toward earlier discovery and management of thyroid cancer and more frequent use of total thyroidectomy and ^{131}I ablation (Schlumberger 1998, Mazzaferri & Kloos 2001, Cooper *et al.* 2006, Pacini *et al.* 2006). Scanning made after a therapy dose of ^{131}I is highly sensitive so that a scan should always be obtained when a therapy dose has been administered. Improved sensitivity of gamma cameras may also be a factor.

We used dual-isotope acquisition of ^{131}I and $^{99\text{m}}\text{Tc}$ -HMDP bone scanning as internal landmarks. The correlation with anatomy can now be rendered easier by combining single-photon emission computed tomography and the computed tomography (^{131}I -SPECT/CT) images were obtained with an integrated system 'hybrid instruments' (Krausz & Israel 2006).

Among the 13 patients with functioning bone metastases, 12 were diagnosed during initial management (clinical work-up or ^{131}I scanning) and one was diagnosed 6 months later. None of the other patients developed functioning bone metastases, in keeping with our previous findings on functioning pulmonary metastases (Hindie *et al.* 2003). These results suggest that post-surgery adjuvant ^{131}I therapy can be useful not only for early diagnosis of distant functioning metastases but possibly also for preventing late metastatic events.

Excellent responses to ^{131}I therapy were obtained, without the need for additional treatment, in six of the eight patients in whom bone metastases were first discovered by ^{131}I scanning. ^{131}I uptake disappeared in five of these patients, while the other patient had slight residual ^{131}I uptake at a single site (the other bone and lung metastases cleared). These results confirm the prognostic importance of early diagnosis of bone metastases of thyroid cancer (Maccocci *et al.* 1989, Pittas *et al.* 2000, Bernier *et al.* 2001, Petrich *et al.* 2001, Haq & Harmer 2005, Durante *et al.* 2006). The only patient who had delayed repeat ^{131}I therapy progressed; MRI became positive and the Tg level increased tenfold. Therefore, when the whole-body ^{131}I scan points to the presence of bone metastases – even if other imaging methods (MRI, CT, etc.) are negative

and the Tg level is only moderately elevated – repeat ¹³¹I therapy should not be postponed; only at this early stage of tiny metastases is there a chance of cure.

In these patients with functional metastases that had no structural correlate on cross-sectional imaging, it is possible that the thyroid cancer metastases are actually bone marrow metastases rather than ‘bone’ metastases *per se*. Since ¹³¹I passes through the bone marrow and the blood stream, and since bone marrow metastases by definition must be quite small, it is likely that ¹³¹I treatment would be more effective in this setting. The 5 mm lesion seen on the MRI in the humerus of patient no.1 was actually in the bone marrow and not in the bone parenchyma.

Antiangiogenic drugs and other targeted treatments may constitute a new therapeutic approach in patients who progress despite ¹³¹I therapy. A number of molecules are under investigation (Baudin & Schlumberger 2007). Yet, none has emerged as providing a definite benefit on survival with acceptable toxicity.

This study suggests that post-surgical ¹³¹I ablation can contribute to early detection of bone metastases, at a time when the Tg level may be only moderately elevated, when other radiological studies are negative, and when the disease is potentially curable by ¹³¹I therapy.

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