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Outcome of Palliative Embolization of Bone Metastases in Differentiated Thyroid Carcinoma

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We investigated the effects of selective embolization in patients with symptomatic bone metastases of differentiated thyroid carcinoma. A total of 41 embolizations was performed in 16 patients. We studied the follow-up (range, 2 months to 8.6 yr) after the first embolization by evaluation of clinical symptoms and tumor dimensions. Success was defined as an improvement in clinical symptoms without tumor progression. The procedure was successful in 24 of 41 occasions (59%). Twenty-six embolizations were preceded or followed up by additional therapies, consisting of surgery (laminectomy), external irradiation, or radioiodine. Subgroup analysis revealed that these additional therapies did not influence the success rate; however, a potential effect on success duration may be present: for embolizations without additional radioiodine or external irradiation therapy, the median success duration was 6.5 months; for embolizations combined with additional radioiodine or external irradiation, this was 15 months (P = 0.0146). The ultimate outcome of the patients was unfavorable: nine patients died and five patients have progressive disease. We concluded that selective embolization of bone metastases may be considered a palliative therapy that may induce rapid, but transient, relief of symptoms. Combination with radioiodine or external irradiation may prolong the duration of success. (*J Clin Endocrinol Metab* 88: 3184–3189, 2003)

DIFFERENTIATED THYROID CARCINOMA has a relatively favorable prognosis, the 10-yr survival being 90–95% (1, 2). This high survival rate is the result of the biological behavior of most of the tumors and the efficacy of primary therapy, consisting of surgery and radioiodine therapy. However, when distant metastases occur, the prognosis is worse because the results of radioiodine therapy, which is virtually the only curative treatment option, are moderate (2, 3): the remission rate in pulmonary metastases treated with radioiodine therapy is about 50%, varying from 90% in patients with microscopic metastases to 10% in macronodular disease (4–7). In bone metastases, remission rates are even worse, varying from 7% to 20% (5–8). A major problem in this category of patients is the diminished ability of thyroid cancer cells to accumulate or incorporate radioiodine, indicated by negative posttherapeutic whole-body scintigraphy. Alternative treatment options like external radiotherapy or chemotherapy have only limited curative success (9). Therefore, treatment options in patients with bone metastases of differentiated thyroid carcinoma are mostly aimed at palliation. Conventional palliative treatment modalities are surgery, when a symptomatic metastatic lesion is accessible to surgery, or external irradiation.

We explored the role of selective embolization of bone metastases as an alternative palliative treatment option. This approach was initially introduced in the management of arteriovenous malformations and preoperative and therapeutic management of well-vascularized benign and malignant tumors (10–12). A review of the literature is given (13). Because embolization can give rapid relief of pain and neurological symptoms in the case of bone metastases, we previously decided to treat four patients with vertebral metastases from follicular carcinoma with this technique (13). Because of the initial success, we extended our series and evaluated the long-term effects of embolization in 16 patients with symptomatic bone metastases of thyroid carcinoma. In our opinion, embolization of bone metastases of differentiated thyroid carcinoma is an attractive palliative therapeutic alternative that may offer rapid, but transient, relief of symptoms.

Abbreviations: CT, Computerized tomography; MRI, magnetic resonance imaging.

Patients and Methods

The Leiden University Medical Center is a large referral center for differentiated thyroid carcinoma in the Netherlands. With the exception of unifocal T1-N0-M0 tumors, initial therapy consists of near-total thyroidectomy followed by routine radioiodine ablative therapy. In the case of recurrent disease or metastases, curative surgery will be attempted if feasible. Radioiodine therapy (6000 MBq) is given when the tumor accumulates radioiodine and repeated if necessary.

Between March 1994 and June 2002, we performed selective embolization in 16 patients with symptomatic bone metastases of differentiated thyroid carcinoma, in which radical surgery was impossible. The group consisted of eight male and eight female patients with a median age of 61 yr at the time of diagnosis. Additional patient characteristics are given in Tables 1 and 2. All patients were initially treated by total thyroidectomy. In all, but two patients (patients 1 and 8), thyroidectomy was followed by radioiodine ablation therapy with a dose of 2800 MBq, or, when surgery was incomplete or metastases were present, 6000 MBq. In patients 1 and 8, the first radioiodine therapy was given after embolization because the bone metastases were the presenting symptom of thyroid carcinoma. Selective embolization of bone metastases was carried out because all patients had symptomatic bone metastases varying from pain to severe spinal cord compression. In these 16 patients, a total of 41 embolizations were performed (Tables 2 and 3), 31 embolizations for vertebral lesions, 8 for pelvical metastases, and 2 for lesions at other sites (Tables 2 and 3). Embolization was performed with an interval of 6 d to 12.3 yr after total thyroidectomy. Seven patients were embolized at least two times, with a maximum of 13 embolizations in patient 11 (two embolizations were performed on the same day and the results of

TABLE 1. Characteristics of 16 patients with bone metastases of differentiated thyroid carcinoma who underwent embolization

Case	Age[a]	Sex	Histology	pTNM class[a,b]	Stage[a,b]	Last follow-up		
							Time after thyroidectomy	Time after first embolization
1	69	M	FTC	T4-N1-M1	IV	Died	4 yr, 6 m	4 yr, 4 m
2	51	M	FTC	Tx-Nx-M0	?	Died	10 yr, 4 m	8 m
3	66	F	FTC	T1-N0-M1	IV	Died	6 yr, 5 m	2 m
4	36	F	FTC	T4-N1-M1	II	Progressive	8 yr, 5 m	2 yr, 10 m
5	72	F	PTC	T4-N0-M1	IV	Died	1 m, 2 wk	3 wk
6	71	F	PTC	T4-N0-M1	IV	Progressive	11 yr, 7 m	1 yr, 11 m
7	62	M	FTC	T4-N0-M0	IV	Died	5 yr, 3 m	4 m
8	60	M	FTC	T2-N0-M1	IV	Died	7 yr, 2 m	7 yr, 2 m
9	60	M	PTC	T4-N1-M0	IV	Died	4 yr, 3 m	2 yr, 8 m
10	53	F	FTC	T2-N0-M0	II	Progressive	9 yr	6 yr, 10 m
11	45	M	FTC	T3-N0-M0	III	Progressive	12 yr, 8 m	8 yr, 8 m
12	74	F	PTC	T2-N0-M1	IV	Regression	5 yr, 3 m	1 yr, 7 m
13	57	F	FTC	T3-N0-M1	IV	Regression	2 yr	1 yr, 6 m
14	72	M	PTC	Tx-N1-M1	IV	Died	1 yr	9 m
15	62	M	PTC	T3-N0-M0	III	Died	8 yr, 6 m	1 yr
16	52	F	FTC	T2-N0-M1	IV	Progressive	1 yr, 5 m	7 m

m, Month; TNM, tumor node metastasis; FTC, follicular thyroid carcinoma; PTC, papillary thyroid carcinoma.
[a] At time of diagnosis.
[b] Postsurgical TNM classification.

these are combined in embolization nr. 5 in Table 2). Additional therapies consisting of radioiodine therapy, external irradiation, or laminectomy were performed before embolization in nine procedures (five patients), after embolization in nine procedures (two patients) and both before and after embolization in eight procedures (seven patients, Tables 2 and 3). More specifically, external irradiation on the skeletal metastases embolized in this study was given before embolization in eight procedures (six patients) and after embolization in seven procedures (six patients). Surgery (laminectomy) for vertebral metastases embolized in this study was performed before embolization in two procedures (two patients) and after embolization in six procedures (three patients). Radioiodine was given within a period of 5 months before embolization in 11 procedures (eight patients) and after embolization in nine procedures (seven patients).

Before and within 6 wk after embolization, a clinical investigation was done consisting of pain assessment as well as a complete neurological examination in case of vertebral metastases. Serum thyroglobulin levels were measured before and after embolization, during continuation of TSH-suppressive T_4 therapy. Tumor dimensions were assessed by magnetic resonance imaging (MRI) or computerized tomography (CT) scan after embolization in 22 embolizations. The radiological dimensions were determined by the measurement of diameter in at least two dimensions.

Successful embolization was defined as an improvement in clinical symptoms for at least 1 month without progression of tumor dimensions at radiological examination (CT or MRI, change in tumor dimensions in two dimensions before and after embolization <25% of original dimensions). Thyroglobulin levels were not included in the criteria for success: an increase in thyroglobulin levels cannot be regarded as proof for an unsuccessful procedure because progression of other metastases could have contributed to this rise. A decrease in thyroglobulin levels without an improvement of clinical symptoms cannot be considered successful palliation. When no radiological examination was performed after embolization, clinical symptoms were used as parameter for success.

The duration of success was defined as the time period evolving after a successful embolization until relapse or worsening of the symptoms occurred related to the embolized metastasis. When no relapse occurred, the duration of success was regarded as the time period between the embolization and the date of last follow-up.

Last known follow-up state was classified as regression (decrease in subsequent thyroglobulin levels greater than 10%, decrease in radiological dimensions ≤ 25%), progressive disease or death (Table 1).

Selective embolization technique

In all patients, serum creatinine levels were checked and if found elevated more than 5% of the upper normal limit, the procedure was not performed. Embolization was performed as follows: after localizing the metastatic lesion by MRI or CT, the feeding arteries were visualized by selective catheterization. When a pathological vascular pattern was recognized and verified that no vital structures were supplied by the particular vessel, particles of polyvinyl alcohol (Ivalon, Laboratoires Nycomed S.A., Paris, France) were injected. The technical success of embolization was verified by angiography performed immediately after the embolization. In case of multiple lesions, only those that were symptomatic or threatening were embolized. The maximum number of lesions that could be embolized within one procedure was approximately five. According to Dutch law, approval from each patient was obtained before embolization, after full explanation of the treatment options, procedures, and potential complications. Palliative embolization of symptomatic tumor metastases is included in the routine clinical care in the Leiden University Medical Center and as such is not considered to be an experimental procedure. Therefore, the procedures described in this study did not require institutional review board approval.

Assays

Thyroglobulin was measured with immunoradiometric assay using the Dynotest TG (Brahms, Berlin, Germany), sensitivity 0.05 mg/ liter, interassay variability 0.3 mg/liter.

Statistics

Data are given individually for all patients. Normally distributed values are summarized as mean ± SD, not normally distributed data as median. Categorical data or proportions are expressed as the number of subjects or embolizations. Differences in not normally distributed data were analyzed with the Mann-Whitney test, categorical variables between subgroups were analyzed with the χ^2 test. A P value of less than 0.05 was considered significant.

Results

All 41 embolization procedures were technically successful. One patient developed a postembolization syndrome, characterized by fever and pain caused by tumor necrosis (patient 8). In one other patient (patient 4), a contrast reaction occurred during the embolization procedure, completely disappearing after treatment with antihistamines. No other complications were observed.

After embolization, there was a rapid relief of pain and neurological symptoms, sometimes within minutes, usually

TABLE 2. Characteristics of embolization procedures in 16 patients with bone metastases of differentiated thyroid carcinoma

Case	Embolization no.	Time after thyroidectomy	Before embolization			After embolization (time after embolization)				Additional therapy	Time relative to embolization[c]
			Symptoms	Tg (μg/liter)	Metastasis embolized	Symptoms[a]	Tg (μg/liter)	X/CT/MRI[a]	Successful[b] (duration of success)		
1	1	2 m	Radicular pain	574	L4	↓	147	↓ (3 m)	Yes (15 m)	Irradiation	+2 m
										Radioiodine	+3 m
	2	1 yr, 5 m	Radicular pain	688	L3	=	152	= (2 m)	No	Radioiodine	−4 d
	3	2 yr, 2 m	Radicular pain	380	L3	↑	464	= (4 m)	No	Laminectomy	+2 m
	4	2 yr, 6 m	Radicular pain, caudal compression	607	L3	=	761		No		
	5	2 yr, 6 m	Radicular pain, caudal compression	607	L2, L3	=	761	= (1 wk)	No	Laminectomy	+13 d
	6	3 yr	Radicular pain	1193	L1, L2, L3	↓	760		Yes (6 m)		
	7	3 yr, 6 m	Radicular pain, hypesthesia	979	L2, L3	↑	979		No		
2	1	9 yr, 6 m	Radicular pain	2524	Th1	↓	4710	↓ (6 m)	Yes (6 m)	Irradiation	−5 m
										Laminectomy	−3 m
										Radioiodine	−1 wk, +7 m
3	1	6 yr, 3 m	Radicular pain	654	Os ischium + os pubis, left side	=	227		No	Irradiation	−7 yr
4	1	5 yr, 7 m	Pain	2271	Manubrium sterni	↓	2060	↑ (3 m)	No	Irradiation	+4 m
										Radioiodine	+7 m
5	1	20 d	Paresis, incontinence	64	Th1	=	Not available		No	Irradiation	−3 m
										Laminectomy	+2 wk
										Irradiation	+3 wk, unsuccessful
6	1	9 yr, 8 m	Radicular pain, cauda compression	971	L3	↓	922	↓ (2 wk)	Yes (23 m)	Radioiodine	−3 m
										Irradiation	+5 m
7	1	4 yr, 11 m	Radicular pain	1081	Th10, Th12	↓	1418		Yes (1 m)		
	2	5 yr	Radicular pain	1418	Th10, Th12	=	959	= (2 wk)	No		
8	1	6 d	Paraplegia, radicular pain	12874	C7	↓	16841	↓ (1 m)	Yes (7 yr)	Irradiation	−3 wk, unsuccessful
										Laminectomy	−2 wk, unsuccessful
										Radioiodine	+3 wk
	2	1 m	Caudal compression	16841	Th7, L2	↓	24583	↑ (2 wk)	No (7 yr)	Radioiodine	+5 m
	3	4 yr, 11 m	Radicular pain	2309	Left acetabulum	↓	3881	↓ (3 m)	Yes (11 m)	Radioiodine	−5 m
										Irradiation	−1 m
	4	5 yr, 10 m	Radicular pain	8630	Pelvis, left side	↓	8500		Yes (16 m)	Radioiodine	−3 m
										Irradiation	+5 m
9	1	1 yr, 7 m	Pain neck, swallow and breathing complaints	65	Paralaryngeal, left side	↑	56	↑ (6 m)	No	Radioiodine	−3 d
										Irradiation	+7 m
10	1	2 yr, 2 m	Radicular pain hypesthesia	267	L1	↓	163		Yes (15 m)	Radioiodine	−3 d
	2	3 yr, 5 m	Radicular pain	508	L1	↓	241		Yes (31 m)	Radioiodine	−3 d
	3	6 yr	Radicular pain, paresthesia	241	L1	↓	237	↓ (2 wk)	Yes (12 m)		

11	1	4 yr	Radicular pain, paraparesis, ataxia	23	Th6	↓	31	↓ (1 m)	Yes (25 m)	Laminectomy	+1 d, unsuccessful
										Irradiation	+2 m
										Radioiodine	+3 m, no uptake
	2	6 yr, 1 m	Radicular pain	79	Th6	↓	58	= (7 m)	Yes (8 m)		
	3	6 yr, 9 m	Radicular pain	111	Th6	↓	108	↓ (7 m)	Yes (6 m)		
	4	7 yr, 3 m	Radicular pain	175	Th5, Th6, Th7	↓	213	↓ (6 m)	Yes (7 m)		
	5	7 yr, 10 m	Radicular pain, paraplegia	311	Th2, Th3, Th5	=	268		No		
	6	8 yr, 1 m	Radicular pain	248	Th1, Th2, Th3, Th5, Th6	=	301	= (2 wk)	No		
	7	8 yr, 2 m	Radicular pain	301	Th1, Th2, Th3	=	540		No	Laminectomy (partial)	+6 d
	8	8 yr, 5 m	Radicular pain	304	Th3, Th5	↓	331	= (1 m)	Yes (2 m)		
	9	8 yr, 7 m	Radicular pain, ataxia	350	Th1, Th2, Th3	=	432	= (5 d)	No		
	10	8 yr, 7 m, 2 wk	Radicular pain	427	Th6	↓	496	= (2 m)	Yes (25 m)	Laminectomy	+1 d
	11	8 yr, 10 m	Radicular pain, paraplegia	767	Th1, Th2, Th3	↓	380		Yes (21 m)	Irradiation	+1 m
	12	12 yr, 4 m	Radicular pain, paraplegia	801	Pelvis	↓	523	= (3 m)	Yes (4 m)		
12	1	3 yr, 8 m	Radicular pain	217	Pelvis	=	117	= (3 m)	No	Radioiodine	−1 m
13	1	5 m, 3 wk	Radicular pain	125100	Os ileum, left side	↓	9640	↓ (3 m)	Yes (13 m)	Radioiodine	−9 d
										Radioiodine	+5 m
	2	1 yr, 6 m	Radicular pain	5291	Os ileum, left side	↓	1806	= (1 wk)	Yes (6 m)	Radioiodine	−1 m
										Radioiodine	+6 m
14	1	2 m, 3 wk	Radicular pain	261	Th9, Th10	=	Not available		No	Radioiodine	−2 m
15	1	7 yr, 6 m	Paraparesis, incontinence	4227	Th10	↓	174		Yes (9 m)	Irradiation	−2 m
	2	8 yr, 3 m	Paraplegia, hypesthesia radicular pain	114	Th9, Th10	↓	127		Yes (3 m)	Irradiation	−2 wk
16	1	10 m		2140	Os pubis, left side	↓	Not available	↓ (6 m)	Yes (7 m)		

M, Month.
[a] ↓, Improvement, normalization; =, no alteration; ↑, progression.
[b] For definition, see *Patients and Methods*.
[c] −, Before embolization; +, after embolization.

TABLE 3. Relation between outcome of embolizations and additional therapies

	Total	Success[a]	Failure		
Radioiodine therapy					
Embolizations preceded by radioiodine therapy (n)	7	4	3		
Embolizations, followed by radioiodine	5	4	1		
Embolizations, preceded and followed by radioiodine	4	3	1		
Total embolizations with radioiodine therapy	16	11	5		$P = 0.414$[b]
Embolizations without radioiodine therapy	25	14	11		
All additional therapies (radioiodine, external irradiation, and/or surgery)					
Embolizations preceded by additional therapies (n)	9	5	4		
Embolizations, followed by additional therapies	9	5	4		
Embolizations, preceded and followed by additional therapies	8	6	2		
Total embolizations with additional therapies	26	16	10		$P = 0.923$[b]
Embolizations without additional therapies	15	9	6		
Duration of success (months)	n	median	min	max	
All embolizations	25	11	1	84	
With additional therapies	16	15,5	3	84	
Without additional therapies	9	6	1	12	$P = 0.003$[b]
With radioiodine	11	15	6	84	
Without radioiodine	14	7	1	25	$P = 0.075$[b]
With external irradiation	10	15	3	84	
Without external irradiation	15	7	1	84	$P = 0.192$[b]
With radioiodine and/or external irradiation	15	15	3	84	
Without radioiodine and/or external irradiation	10	6,5	1	25	$P = 0.0146$[b]

[a] For definition, see *Patients and Methods*.
[b] χ^2 test.

within 1 d, in 26 of a total of 41 procedures. In 11 procedures, symptoms remained stable, whereas in three procedures, the patient had progressive symptoms. In seven patients neurological symptoms other than pain were present. Successful embolizations improved all neurological symptoms, except embolizations 11 and 12 in patient 11, that relieved pain but not the paraplegia.

Radiological examination was performed after 22 procedures and demonstrated a reduction of tumor size in 11 cases. In seven cases, the tumor was stable and in four tumor size increased. Serum thyroglobulin levels decreased after 20 and increased after 16 embolizations. Overall, there was a median decrease in serum thyroglobulin levels of 6.5 μg/liter.

According to the criteria for success as defined in *Patients and Methods,* 24 of 41 (59%) embolization procedures were successful (Tables 2 and 3). In two embolizations (patients 4 and 8, second embolization), symptoms improved, whereas tumor dimensions increased. According to the criteria, these were considered unsuccessful.

No differences in success rates were observed between embolization procedures that were or were not preceded or followed by surgery, radioiodine, and/or external irradiation. The results for all additional therapies as well as radioiodine are given in Table 3.

The duration of success showed a considerable intra- and interindividual variation. The median duration of efficacy was 11 months (range, 1–84). There was a significant difference between embolizations without and with additional therapies: the median duration of effectiveness in embolizations combined with other therapies was 15.5 months (3–84 months), in embolizations without additional therapies only 6 months (1–12 months) (Table 3). This difference was not explained by the presence or absence of additional radioiodine therapies. However, when success duration was compared between embolizations with and without radioiodine therapy and/or external irradiation, the difference in success duration was significant (Table 3). Overall, relapses of symptoms recurred within 4–12 months after the preceding embolization.

During follow-up, nine patients died, and five patients have progressive disease. Only two patients are currently in sustained regression.

Discussion

Our data indicate that embolization is an immediately effective, palliative treatment in 59% of the procedures. However, the data also indicate that this palliative effect is transient. In the absence of additional therapies, symptoms recurred after approximately 6 months. This interval was increased, when additional palliative treatments were included.

Curative therapeutic options in patients with bone metastases of differentiated thyroid carcinoma are limited, especially when there is no uptake of radioiodine. Nevertheless, these patients will have a life expectancy that may extend for several years. As a consequence, these patients may be exposed to the burden of symptomatic metastases for a long period of time, necessitating the need for palliative therapy. Surgery, external irradiation, and to a lesser extent radioiodine therapy are the conventional palliative treatment modalities in these patients. Because many bone metastases of thyroid carcinoma do not accumulate iodine and the effect of radioiodine therapy is not rapid, radioiodine therapy is of limited use as a palliative treatment option. Surgery may lead to rapid relief of symptoms but is possible only when the metastasis is approachable, can be technically complicated, and is always burdensome for the patient. External irradiation is the most frequently applied palliative therapy in bone metastases of thyroid carcinoma. Although this therapy can

be effective, limiting factors may be the radiosensitivity of the tumor and the site of the tumor: in vertebral metastases, the maximal radiation dose is limited by the proximity of the spinal cord. Selective embolization of tumor metastases is another option, which is especially effective to induce an immediate relief of pain and neurological symptoms. The procedure can be repeated many times, is relatively easy to perform, and is not very burdensome for the patient.

In 10 patients, at least one successful procedure was performed. It can be questioned whether the presence of additional therapies may have contributed to the success of embolizations or even that the success of embolization combined with other therapies may be entirely attributed to these additional therapies. However, subgroup analysis did not reveal a difference in success rate between embolizations combined or not combined with other therapies (Table 3). In embolizations without additional therapies, the success rate was identical. In addition, successful embolizations were mostly accompanied by an acute improvement in symptoms that cannot be explained by the additional therapies. However, we found an indication that additional therapies influenced the median duration of success, which was longer when embolizations were combined with additional therapies, specifically radioiodine therapy and/or external irradiation. From a theoretical point of view, embolization and irradiation may have additive effects: oxygen deprivation after embolization is a major stimulus for tumor-induced neovascularization and tumor relapse (14). Irradiation may prevent this effect. However, because the additional therapies have not been performed in a randomized fashion, the results as observed in this study have to be interpreted with caution.

Obviously, the success of embolization depends on the completeness of the obstruction in the arterial supply of the particular bone metastasis. In 18 of 22 occasions in which a CT scan was performed, there was a reduction in tumor size or stabilization after embolization.

We did not observe any irreversible complications of selective embolization in our series. Only one patient suffered from a so-called postembolization syndrome, characterized by fever and pain caused by tumor necrosis. In another patient, a reaction to contrast occurred during the embolization procedure. Technical complications, like arteriovenous fistula, aneurysm at the puncture site, or cholesterol emboli did not occur in our study.

In conclusion, selective embolization of bone metastases of differentiated thyroid carcinoma is especially effective in inducing a rapid relief of pain and neurological symptoms in about 60% of occasions. Combination with additional therapies does not appear to influence this percentage but may prolong the duration of the effect.

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References

1. **Hundahl SA, Fleming ID, Fremgen AM, Menck HR** 1998 A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985–1995. Cancer 83:2638–2648
2. **Mazzaferri EL, Kloos RT** 2001 Clinical review 128: current approaches to primary therapy for papillary and follicular thyroid cancer. J Clin Endocrinol Metab 86:1447–1463
3. **Schaap J, Eustatia-Rutten CF, Stokkel M, Links TP, Diamant M, van der Velde EA, Romijn JA, Smit JW** 2002 Does radioiodine therapy have disadvantageous effects in non-iodine accumulating differentiated thyroid carcinoma? Clin Endocrinol (Oxf) 57:117–124
4. **Samaan NA, Schultz PN, Haynie TP, Ordonez NG** 1985 Pulmonary metastasis of differentiated thyroid carcinoma: treatment results in 101 patients. J Clin Endocrinol Metab 60:376–380
5. **Ruegemer JJ, Hay ID, Bergstralh EJ, Ryan JJ, Offord KP, Gorman CA** 1988 Distant metastases in differentiated thyroid carcinoma: a multivariate analysis of prognostic variables. J Clin Endocrinol Metab 67:501–508
6. **Pacini F, Cetani F, Miccoli P, Mancusi F, Ceccarelli C, Lippi F, Martino E, Pinchera A** 1994 Outcome of 309 patients with metastatic differentiated thyroid carcinoma treated with radioiodine. World J Surg 18:600–604
7. **Schlumberger M, Challeton C, De Vathaire F, Travagli JP, Gardet P, Lumbroso JD, Francese C, Fontaine F, Ricard M, Parmentier C** 1996 Radioactive iodine treatment and external radiotherapy for lung and bone metastases from thyroid carcinoma. J Nucl Med 37:598–605
8. **Marcocci C, Pacini F, Elisei R, Schipani E, Ceccarelli C, Miccoli P, Arganini M, Pinchera A** 1989 Clinical and biologic behavior of bone metastases from differentiated thyroid carcinoma. Surgery 106:960–966
9. **Haugen BR** 1999 Management of the patient with progressive radioiodine non-responsive disease. Semin Surg Oncol 16:34–41
10. **Guibaud L, Herbreteau D, Dubois J, Stempfle N, Berard J, Pracros JP, Merland JJ** 1998 Aneurysmal bone cysts: percutaneous embolization with an alcoholic solution of zein—series of 18 cases. Radiology 208:369–373
11. **Gold RE, Grace DM** 1975 Gelfoam embolization of the left gastric artery for bleeding ulcer: experimental considerations. Radiology 116:575–580
12. **Sun S, Lang EV** 1998 Bone metastases from renal cell carcinoma: preoperative embolization. J Vasc Interv Radiol 9:263–269
13. **Smit JW, Vielvoye GJ, Goslings BM** 2000 Embolization for vertebral metastases of follicular thyroid carcinoma. J Clin Endocrinol Metab 85:989–994
14. **Rockwell S** 1997 Oxygen delivery: implications for the biology and therapy of solid tumors. Oncol Res 9:383–390