



8 Ulusal Endokrin Cerrahi Kongresi

27-30 Nisan 2017 Gloria Kongre Merkezi ANTALYA

RADYOAKTİF İYOT TEDAVİSİ Kime ? Ne Kadar ?

Dr. Seyfettin ILGAN

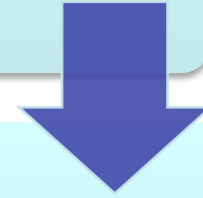


Sunu Planı

- Tiroid kanserinde kanıta dayalı tıp ve rehberler
- Radyoaktif iyotun rolü niye değişiyor
- ATA 2015 vs Nükleer tıp (EANM) rehberi
- Risk gruplarına göre iyot kullanımı
- İyot yan etkileri
- Hariç tutulanlar
 - Dozimetri teknikleri
 - İyot I-131 tedavi hazırlığı
 - Thyrogen vs T4 off

Tiroid Kanserinde Tedavi

Cerrahi



I-131 Ablasyon / Tedavi

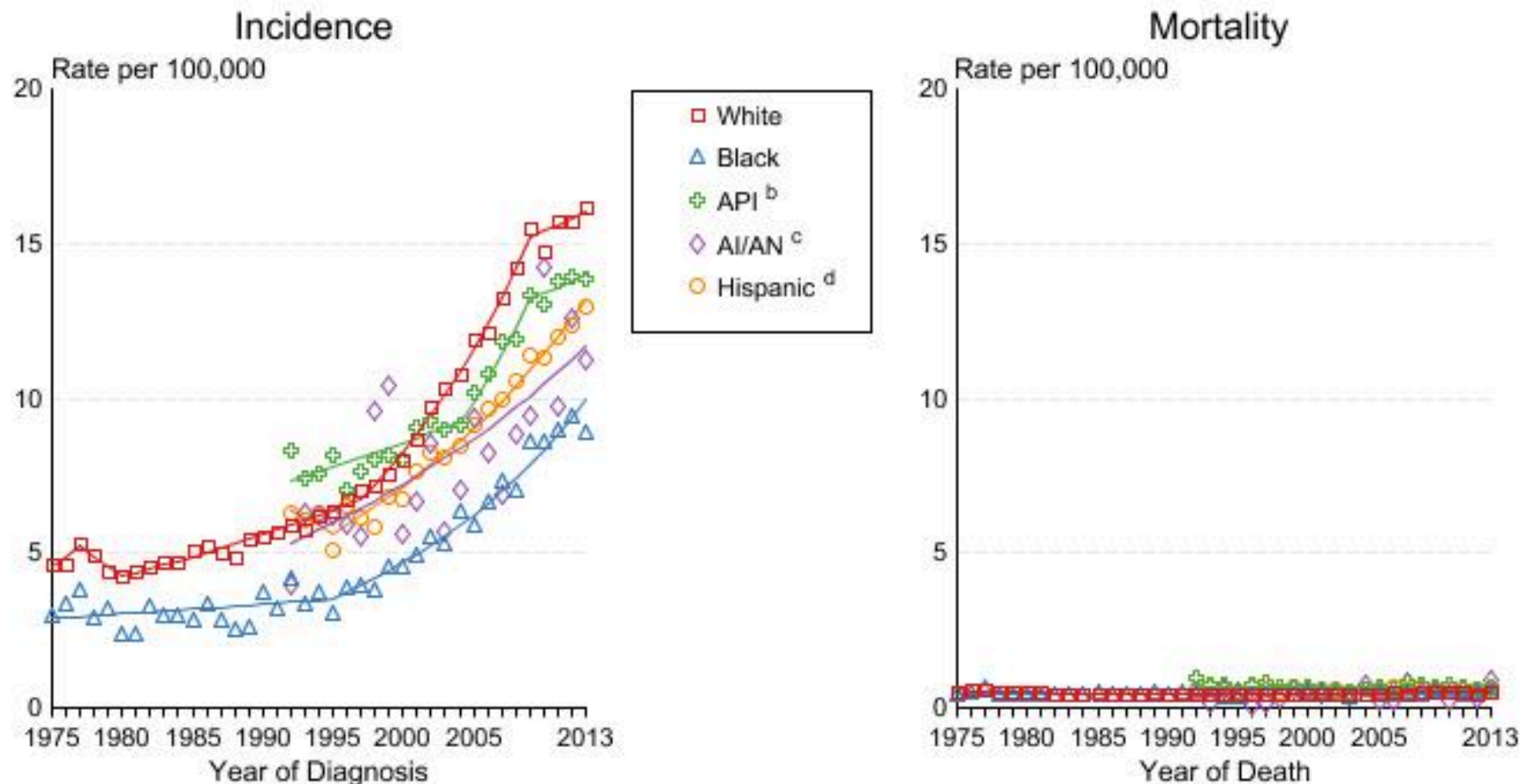


TSH supresyonu

SEER Incidence and US Death Rates^a Cancer of the Thyroid, Both Sexes

Joinpoint Analyses for Whites and Blacks from 1975-2013

and for Asian/Pacific Islanders, American Indians/Alaska Natives and Hispanics from 1992-2013



Source: Incidence data for whites and blacks are from the SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta). Incidence data for Asian/Pacific Islanders, American Indians/Alaska Natives and Hispanics are from the SEER 13 Areas (SEER 9 Areas, San Jose-Monterey, Los Angeles, Alaska Native Registry and Rural Georgia). Mortality data are from US Mortality Files, National Center for Health Statistics, CDC.

^a Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

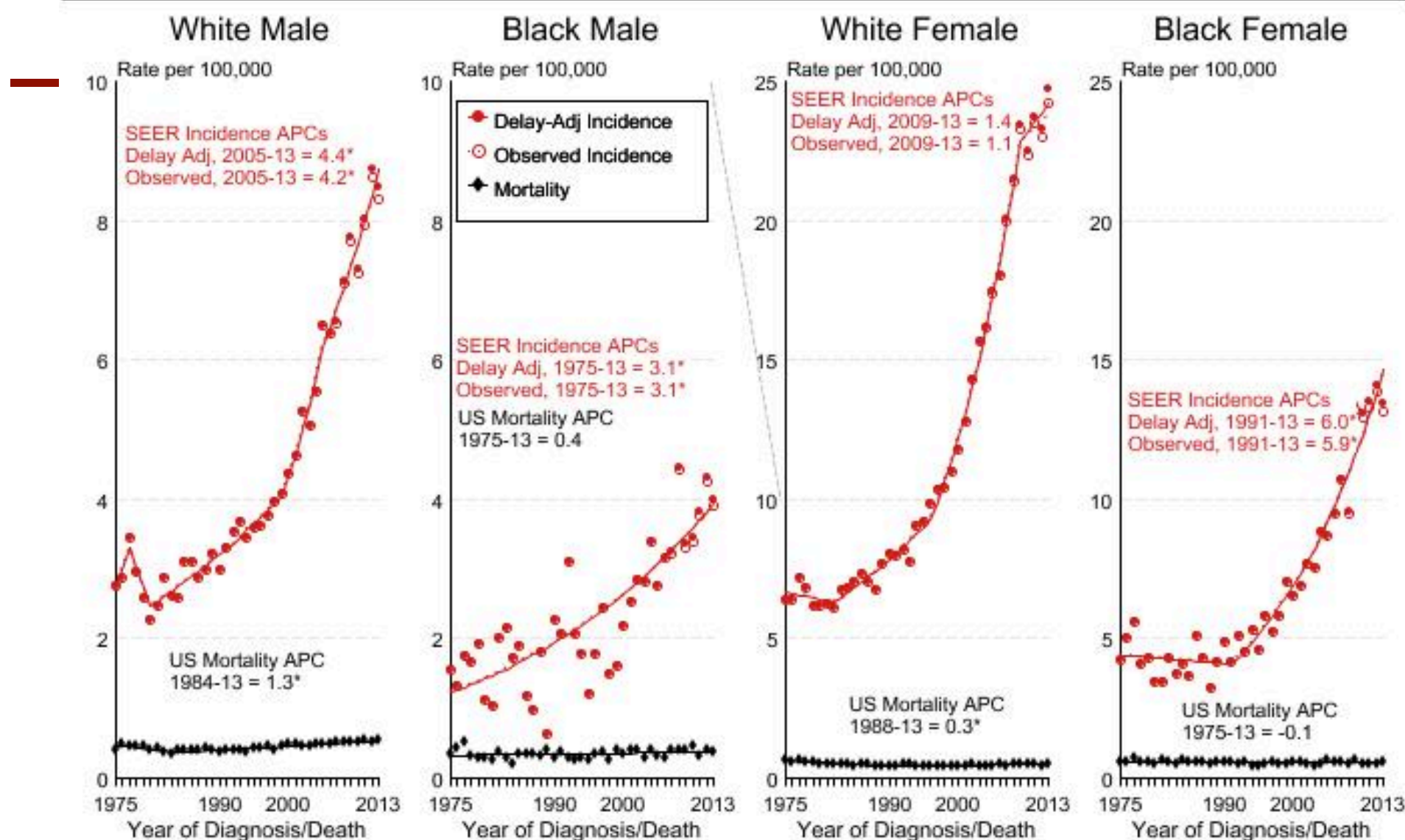
Regression lines are calculated using the Joinpoint Regression Program Version 4.3.0.0, April 2016, National Cancer Institute. Joinpoint analyses for Whites and Blacks during the 1975-2013 period allow a maximum of 5 joinpoints. Analyses for other ethnic groups during the period 1992-2013 allow a maximum of 4 joinpoints.

^b API = Asian/Pacific Islander.

^c AI/AN = American Indian/Alaska Native. Rates for American Indian/Alaska Native are based on the CHSDA (Contract Health Service Delivery Area) counties.

^d Hispanic is not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives. Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry. Mortality data for Hispanics exclude cases from New Hampshire and Oklahoma.

SEER Observed Incidence, SEER Delay Adjusted Incidence and US Death Rates^a Cancer of the Thyroid, by Race and Sex



Source: SEER 9 areas and US Mortality Files (National Center for Health Statistics, CDC).

^a Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).

Regression lines and APCs are calculated using the Joinpoint Regression Program Version 4.3.0.0, April 2016, National Cancer Institute.

The APC is the Annual Percent Change for the regression line segments. The APC shown on the graph is for the most recent trend.

* The APC is significantly different from zero ($p < 0.05$).

Tiroid kanserinde kanıta dayalı yaklaşım

- Prognoz mükemmel / çalışma süreleri çok uzun (10-60 yıl)
- Tedavi farklılıklarının mortalite ve rekürrense etkisi ?
- Randomize kontrollü çalışma az
- Heterojen çalışma grupları
 - Tedavi (cerrahi, I-131, radyoterapi)
 - Takip stratejilerinde önemli değişim
- Son 10-15 yılda yaygın US kullanımı sonucu gruplarda
 - non-insidental PMC sayısında hızlı artış
 - rekürrenslerin tespiti kolay

Rehberler Ne Kadar Önemli ?

- Nükleer tıp dışı disiplinler için temel referans ATA Rehberi
- Ablasyon amaçlı I-131 kullanımını caydırıcı öneriler
- Birçok olguda I-131 kullanımı belirsiz
- Düşük ve orta risk grubundaki bir çok hasta grubu için ablasyon ve adjuvan tedavide “consider” önerisi
 - %42 – 2015 ATA Rehberi
 - %28.6 – 2009 ATA Rehberi

ATA - 2009

TABLE 5. MAJOR FACTORS IMPACTING DECISION MAKING IN RADIOIODINE REMNANT ABLATION

Factors	Description	Expected benefit			RAI ablation usually recommended	Strength of evidence
		Decreased risk of death	Decreased risk of recurrence	May facilitate initial staging and follow-up		
T1	1 cm or less, intrathyroidal or microscopic multifocal	No	No	Yes	No	E
	1–2 cm, intrathyroidal	No	Conflicting data ^a	Yes	Selective use ^a	I
T2	>2–4 cm, intrathyroidal	No	Conflicting data ^a	Yes	Selective use ^a	C
T3	>4 cm					
	<45 years old	No	Conflicting data ^a	Yes	Yes	B
	≥45 years old	Yes	Yes	Yes	Yes	B
	Any size, any age, minimal extrathyroidal extension	No	Inadequate data ^a	Yes	Selective use ^a	I
T4	Any size with gross extrathyroidal extension	Yes	Yes	Yes	Yes	B
Nx,N0	No metastatic nodes documented	No	No	Yes	No	I
N1	<45 years old	No	Conflicting data ^a	Yes	Selective use ^a	C
	>45 years old	Conflicting data	Conflicting data ^a	Yes	Selective use ^a	C
M1	Distant metastasis present	Yes	Yes	Yes	Yes	A

^aBecause of either conflicting or inadequate data, we cannot recommend either for or against RAI ablation for this entire subgroup. However, selected patients within this subgroup with higher risk features may benefit from RAI ablation (see modifying factors in the text).

ATA 2015 – 101 Öneri – 179 Alt Öneri

Öneri / Kanıt Kalite Düzeyi	Yüksek	Orta	Düşük	Yetersiz
Güçlü Öneri	6	65	29	-
Zayıf Öneri	-	10	58	-
Öneri Yok	-	-	1	10
	6	75	88	10

Öneri / Kanıt Kalite Düzeyi	Yüksek	Orta	Düşük	Yetersiz
Güçlü Öneri	%3	%36	%16	-
Zayıf Öneri	-	%6	%32	-
Öneri Yok	-	-	%1	%6

Güçlü öneri / yüksek kaliteli kanıt

- Bilinen/şüpheli metastatik olguda lenf nodları US ile değerlendirilmeli
- Tiroid nodüllerinin değerlendirilmesinde tercih edilen yöntem İİAB
- Benign sitolojide başka tanısal çalışma ve tedavi gerekmez
- Benign nodüllerde rutin TSH supresyonu önerilmez
- Düşük risk grubunda veya düşük risk özellikleri olan orta risk grubunda I-131 remnant ablasyonu yapılırsa düşük doz (30 mCi) yüksek doza tercih edilmelidir
- Serum Tg ve Anti Tg birlikte ölçülmeli, ideal olarak aynı laboratuvar ve yöntemle izlenmelidir

Düşük Risk Grubu

TABLE 14. CHARACTERISTICS ACCORDING TO THE AMERICAN THYROID ASSOCIATION RISK STRATIFICATION SYSTEM AND AJCC/TNM STAGING SYSTEM THAT MAY IMPACT POSTOPERATIVE RADIOIODINE DECISION-MAKING

<i>ATA risk Staging (TNM)</i>	<i>Description</i>	<i>Body of evidence suggests RAI im- proves disease- specific survival?</i>	<i>Body of evidence suggests RAI im- proves disease- free survival?</i>	<i>Postsurgical RAI indicated?</i>
ATA low risk T1a N0,Nx M0,Mx	Tumor size ≤1 cm (uni-or multi- focal)	No	No	No
ATA low risk T1b,T2 N0, Nx M0,Mx	Tumor size >1–4 cm	No	Conflicting observational data	Not routine ^b —May be considered for patients with aggressive histology or vascular invasion (ATA intermedi- ate risk).

TABLE 14. CHARACTERISTICS ACCORDING TO THE AMERICAN THYROID ASSOCIATION RISK STRATIFICATION SYSTEM AND AJCC/TNM STAGING SYSTEM THAT MAY IMPACT POSTOPERATIVE RADIOIODINE DECISION-MAKING

<i>ATA risk Staging (TNM)</i>	<i>Description</i>	<i>Body of evidence suggests RAI im- proves disease- specific survival?</i>	<i>Body of evidence suggests RAI im- proves disease- free survival?</i>	<i>Postsurgical RAI indicated?</i>
ATA low to in- termediate risk T3 N0,Nx M0,Mx	Tumor size >4cm	Conflicting data	Conflicting observational data	Consider ^b —Need to consider presence of other adverse features. Advancing age may favor RAI use in some cases, but specific age and tumor size cutoffs subject to some uncertainty. ^a
ATA low to in- termediate risk T3 N0,Nx M0,Mx	Microscopic ETE, any tumor size	No	Conflicting observational data	Consider ^b —Generally favored based on risk of recurrent disease. Smaller tumors with microscopic ETE may not require RAI.
ATA low to in- termediate risk T1-3 N1a M0,Mx	Central compart- ment neck lymph node metastases	No, except possi- bly in subgroup of patients ≥45 years of age (NTCTCSG Stage III)	Conflicting observational data	Consider ^b —Generally favored, due to somewhat higher risk of persistent or recurrent disease, especially with increasing number of large (>2–3 cm) or clinically evident lymph nodes or presence of extra-nodal extension. Advancing age may also favor RAI use. ^a However, there is insufficient data to mandate RAI use in patients with few (<5) microscopic nodal metastases in central compartment in absence of other adverse features.
ATA low to in- termediate risk T1-3 N1b M0,Mx	Lateral neck or mediastinal lymph node metastases	No, except possi- bly in subgroup of patients ≥45 years of age	Conflicting observational data	Consider ^b —Generally favored, due to higher risk of persistent or recurrent disease, especially with increasing number of macroscopic or clinically evident lymph nodes or presence of extranodal extension. Advancing age may also favor RAI use. ^a

Yüksek Risk Grubu

TABLE 14. CHARACTERISTICS ACCORDING TO THE AMERICAN THYROID ASSOCIATION RISK STRATIFICATION SYSTEM AND AJCC/TNM STAGING SYSTEM THAT MAY IMPACT POSTOPERATIVE RADIOIODINE DECISION-MAKING

<i>ATA risk Staging (TNM)</i>	<i>Description</i>	<i>Body of evidence suggests RAI im- proves disease- specific survival?</i>	<i>Body of evidence suggests RAI im- proves disease- free survival?</i>	<i>Postsurgical RAI indicated?</i>
ATA high risk T4 Any N Any M	Any size, gross ETE	Yes, observational data	Yes, observational data	Yes
ATA high risk M1 Any T Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

I-131 Doz Seçimi

- Kantitatif Kan/Tüm Vücut Dozimetri
 - Tolere edilebilir maksimum kemik iliği/akciğer dozu
 - Kemik iliği dozu < 2 Gy,
 - 48. saatte WB retansiyonu 120 mCi
 - Diffüz akciğer veya kemik metastazı var ise 48. saatte WB retansiyonu 80 mCi
- Kantitatif Tümör Dozimetri
 - 30.000 cGy tiroid remnantı için (%80 ablasyon)
 - 8.000-12.000 cGy lenf nodu/yumuşak doku met (%80 kontrol)
- Uptake Çalışması ile Doz Seçimi
 - 30.000 cGy remnant doz hesaplaması
- Fiks / Ampirik / Standart Doz Uygulaması

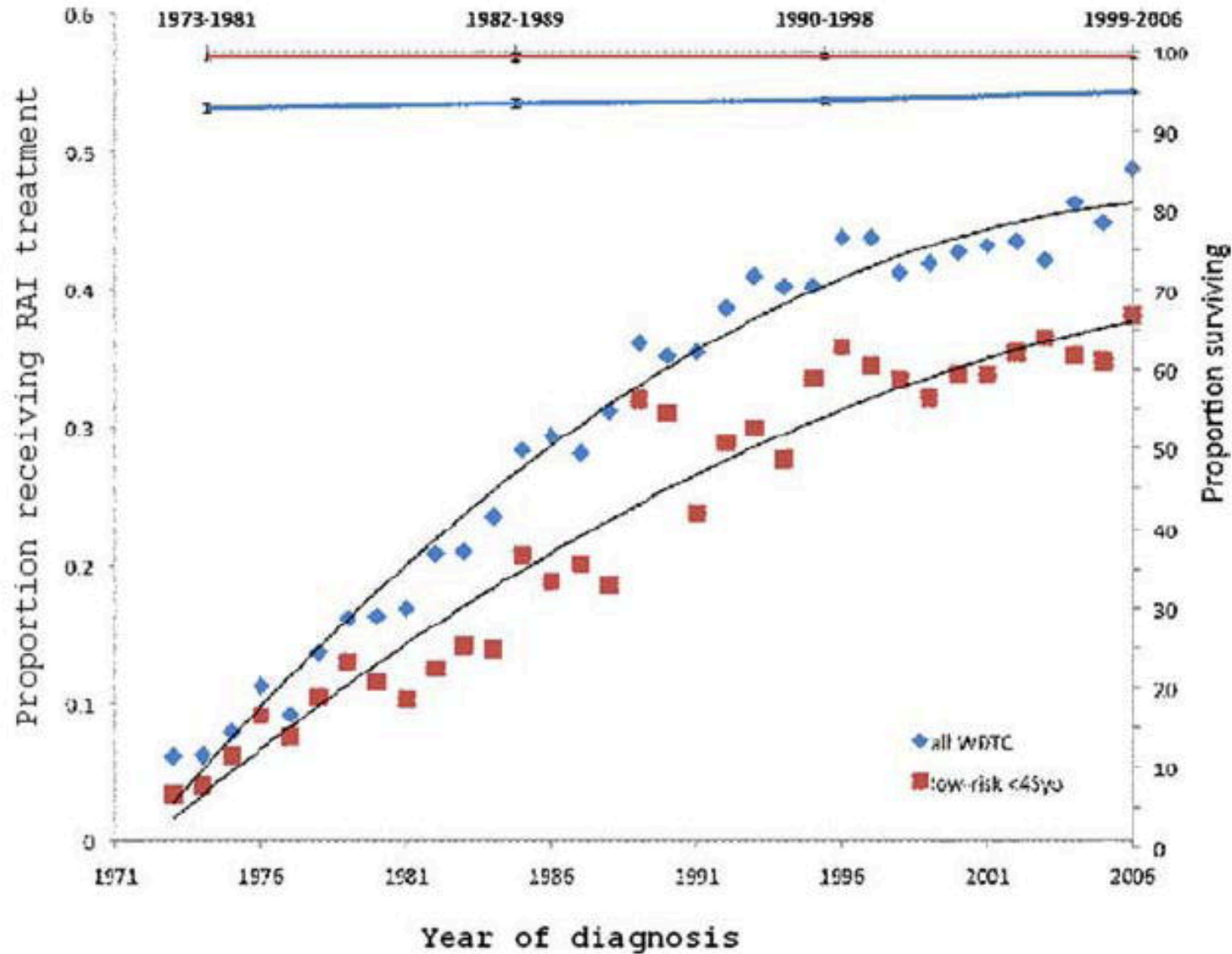
I-131 Doz Seçimi

- Tiroidektomi sonrası ilk I-131 Uygulaması
 - Düşük risk T1N0M0 30-100 mCi
 - Standart risk 100-150 mCi
 - Yüksek risk T4/M1/sınır +
rezidüel nod veya tümör 200 mCi
- Tekrar I-131 Tedavi Uygulaması
 - Sadece Tg yüksekliği 150 mCi
 - Rezidüel malignite 200 mCi

Tiroid kanserinde neler değişiyor?

- Küçük tümörlerde aktif izlem
- T1-2 tümörlerde lobektomi
- Düşük/orta risk grubunda daha sık cerrahi kür
- I-131 kullanımı azalıyor ?
 - Tanısal
 - Ablasyon/Tedavi

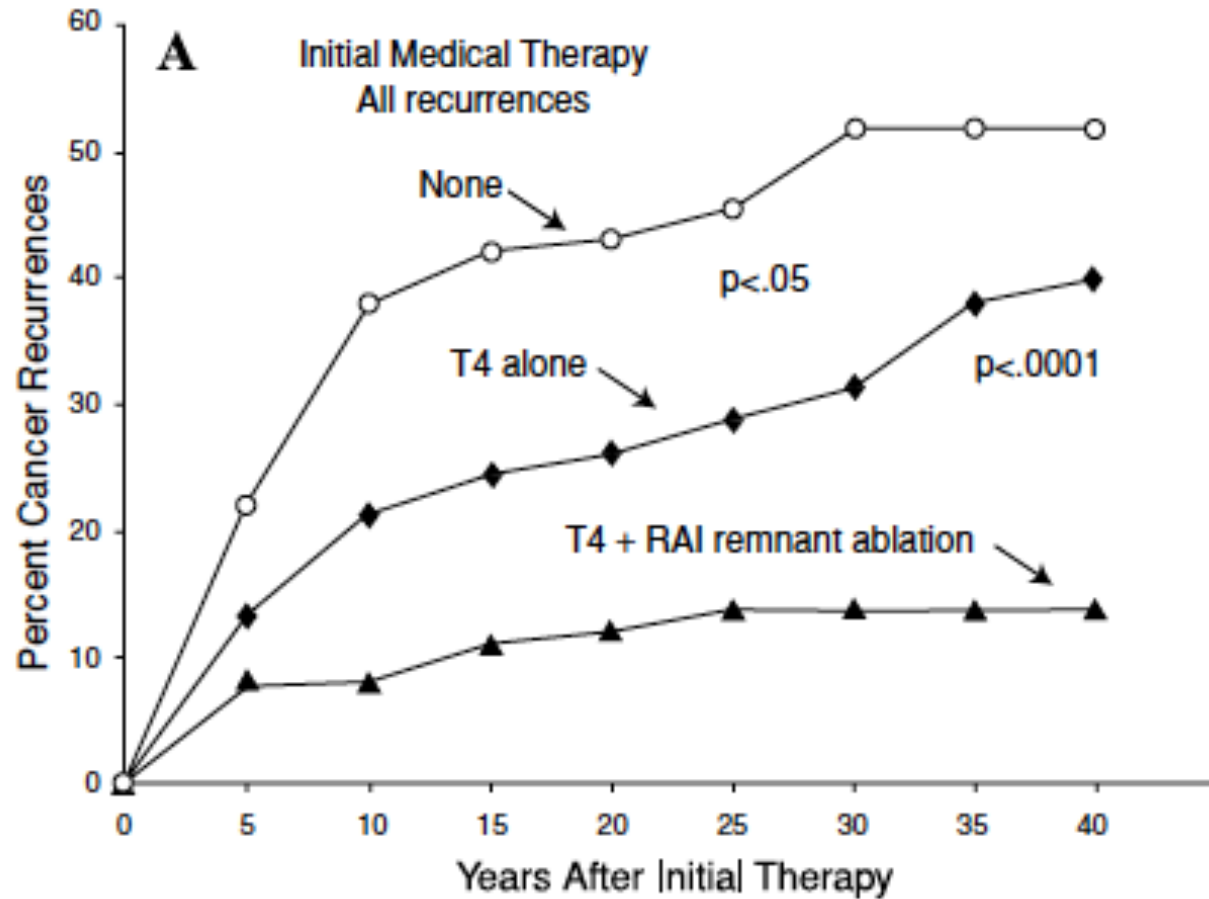
I-131 kullanımı azalıyor mu ?



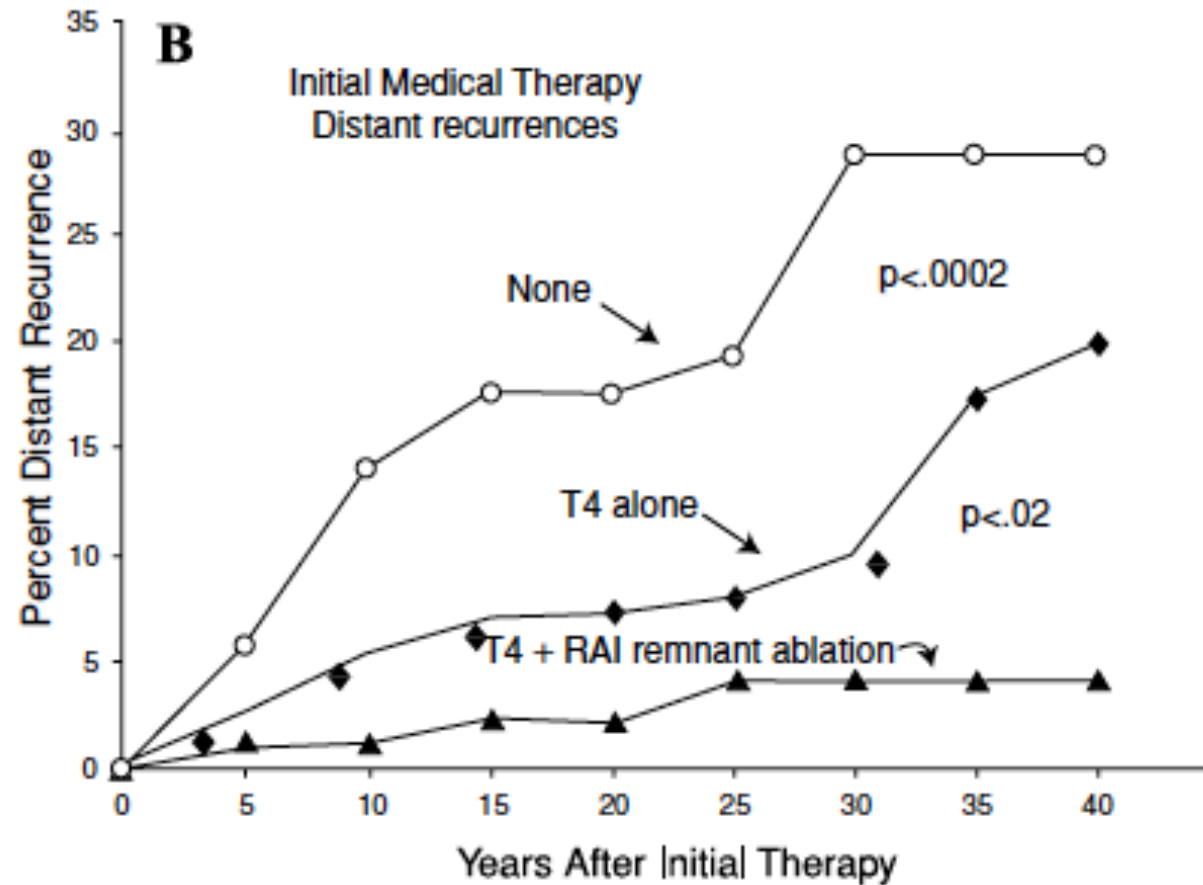
I-131 Kullanımı Önerisi Neden Azalıyor ?

- Etkisiz ?
- Katkısı yok ?
- Yan etkileri çok fazla ?

Etkisiz mi ?



Etkisiz mi ?



Radioactive Iodine Therapy: Effect On Functioning Metastases of Adenocarcinoma of the Thyroid

S.M. Seidlin, MD
L.D. Marinelli, MA
Eleanor Oshry

Therapy of neoplastic disease usually consists of two phases: first, the treatment of the primary focus and, second, that of metastases. Specifically, in adenocarcinoma of the thyroid, the primary site together with its immediate extensions is conventionally treated by surgery, radiation, or both. Distant metastases, if treated, are usually subjected to palliative external irradiation. This paper is a report of successful

therapy of a case of metastatic adenocarcinoma of the thyroid treated by the principle of specific internal irradiation with radioactive iodine.

The earliest study of the uptake of radioactive iodine in two cases of carcinoma was reported by Hamilton and his associates in 1940. In 1942 he described two metastases in which tracer doses of radioactive iodine had been given to the patients prior to the removal of carcinomatous thyroids. Radioautographs of the excised glands showed no significant deposition of the radioactive iodine in malignant areas in any of these cases.

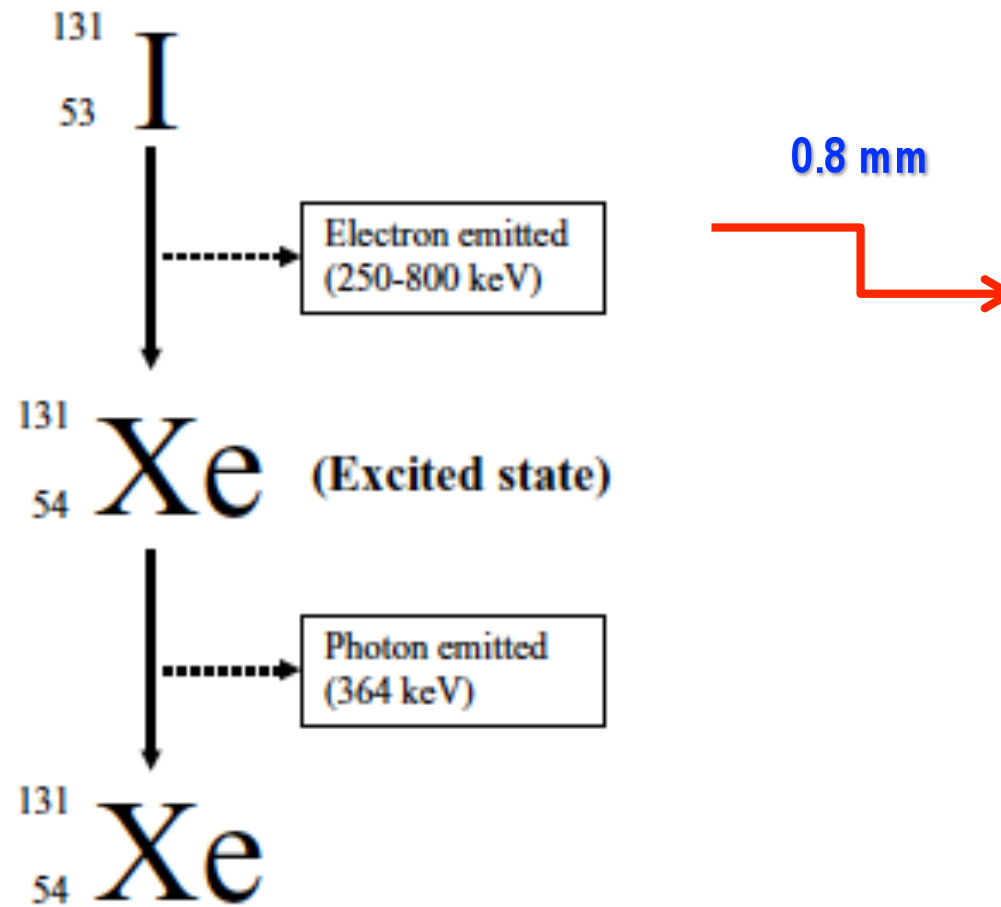
In April 1942, Keston, Ball, Frantz and Palmer reported the first positive evidence of pickup of the radioactive iodine by a metastasis from a carcinoma of the thyroid. In a patient with multiple lesions, Geiger counter measurements showed appreciable uptake of radioactive iodine in only one of the metastases. Subsequently, from the autopsy, these authors⁴ reported that "the bulk of the metastatic tissue was undifferentiated. The metastasis that showed consistent uptake of iodine was the only one that grossly resembled thyroid tissue and that, microscopically, showed chiefly well

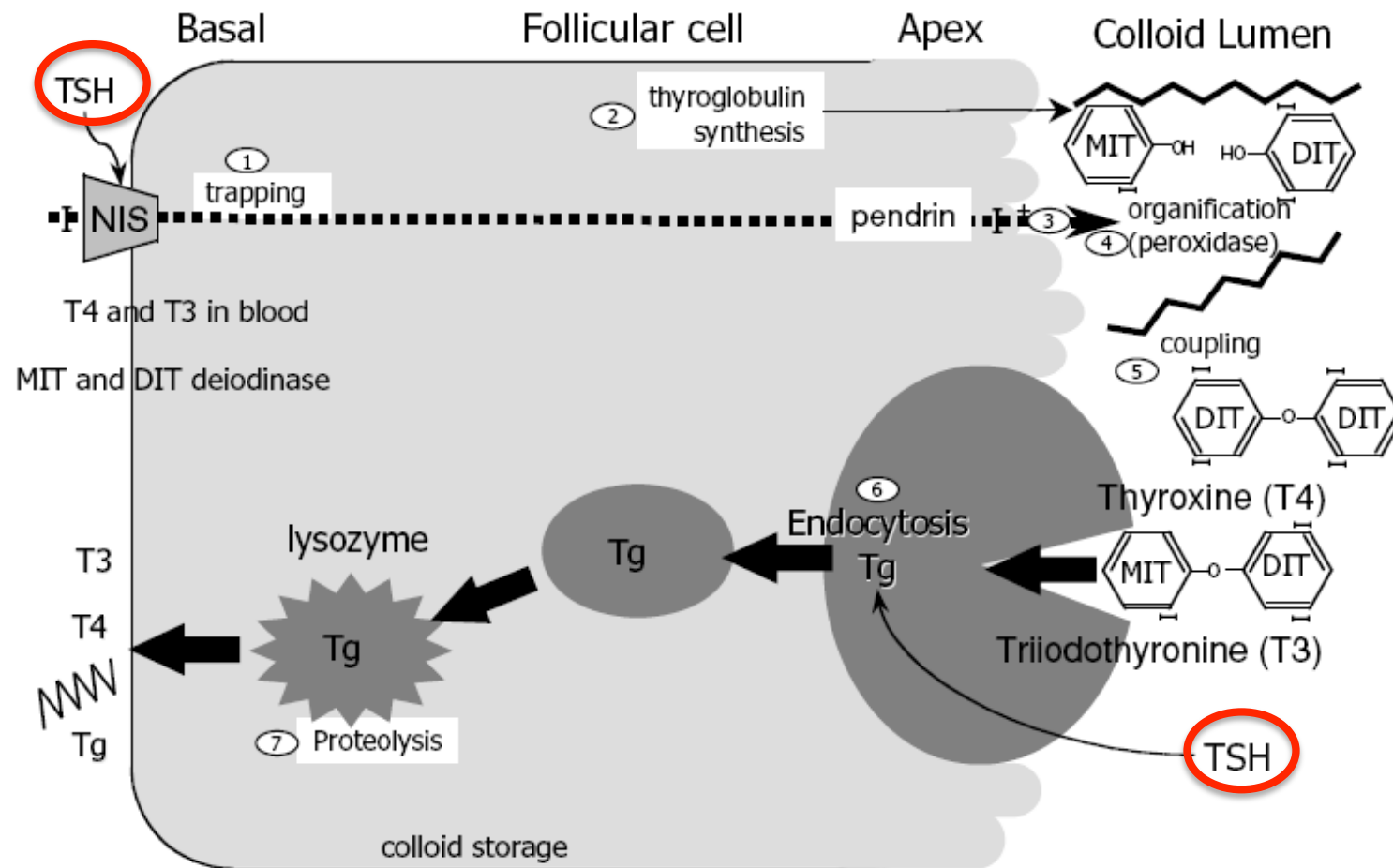
At the time this paper was published the authors were affiliated with the Medical Division of Montefiore Hospital and the Physics Department of Montefiore Hospital and the Physics Department of Memorial Hospital in New York, New York.

Reprinted with permission from Journal of the American Medical Association 132:838-847, 1946. Copyright 1946, American Medical Association.

A preliminary report of this work was presented at the Clinical Research Meeting of the New York Academy of Medicine on May 16, 1945. Aided by grants from the Hazen Foundation for Medical Research and from the Lederle Laboratories to Dr. Seidlin at Montefiore Hospital. The cooperation of the staffs of the Massachusetts Institute of Technology and Washington University cyclotrons and of Dr. R.D. Evans made this work possible. Dr. Louis Leiter, Chief of the Medical Division of Montefiore Hospital,

I-131





I-131 Yarılanma Süresi

	I-131 Biyolojik Yarı-ömür		I-131 Efektif Yarı-ömür	
I-131 Fizik Yarı-ömür	Tiroid	Ekstratiroidal	Tiroid	Ekstratiroidal
8 Gün	80 gün	12 gün	7.3 gün	8 saat

I-131 Konsantrasyonuna Göre Sınıflama

- I-131 (+)

- *Papiller karsinom*
 - Klasik tip
 - Folliküler varyant
 - Diffüz sklerozan varyant
- *Folliküler karsinom*

- I-131 (-/+)

- *Papiller karsinom*
 - Tall cell varyant
 - Kolumnar hücreli varyant
- *Hürthle hücreli karsinom*
- *Az diferansiye (insuler) karsinom*

- I-131 (-)

- *Anaplastik karsinom*
- *Medüller karsinom*

Neden I-131 Uyguluyoruz ?

- Remnant ablasyonu
 - Başlangıç evrelemesini ve rekürren hastalığın tespitini kolaylaştırmak
 - Tg, I-131 tüm vücut tarama
- Adjuvan Tedavi
 - Rekürrens riski yüksek olan olgularda hastalığa özgü sağkalım ve hastalıksız sağkalım süresini iyileştirmek
 - kanıtlanmamış, şüpheli tümör odaklarını yok etmek
- Tedavi
 - Yüksek risk grubunda hastalığa özgü sağkalım ve hastalıksız sağkalım süresini iyileştirmek
 - Rezidüel hastalığı yok etmek

Neden I-131 Uyguluyoruz ?

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 - Tg, I-131 tüm vücut tarama
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 - Rezidüel hastalığı yok etmek

Yüksek Risk Grubunda I-131 Kullanımı

TEDAVİ

ATA 2015

[B36] What is the role of RAI (including remnant ablation, adjuvant therapy, or therapy for persistent disease) after thyroidectomy in the primary management of DTC?

(E) RAI adjuvant therapy is routinely recommended after total thyroidectomy for ATA high risk DTC patients

(Strong recommendation, Moderate-quality evidence)

ATA - 2015

TABLE 11. ATA 2009 RISK STRATIFICATION SYSTEM WITH PROPOSED MODIFICATIONS

ATA low risk	Papillary thyroid cancer (with all of the following): • No local or distant metastases; • All macroscopic tumor has been resected • No tumor invasion of loco-regional tissues or structures • The tumor does not have aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma) • If ^{131}I is given, there are no RAI-avid metastatic foci outside the thyroid bed on the first posttreatment whole-body RAI scan • No vascular invasion • Clinical N0 or ≤ 5 pathologic N1 micrometastases (< 0.2 cm in largest dimension)^a Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer^a Intrathyroidal, well differentiated follicular thyroid cancer with capsular invasion and no or minimal (< 4 foci) vascular invasion^a Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including <i>BRAF</i>^{V600E} mutated (if known)^a
ATA intermediate risk	Microscopic invasion of tumor into the perithyroidal soft tissues RAI-avid metastatic foci in the neck on the first posttreatment whole-body RAI scan Aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma) Papillary thyroid cancer with vascular invasion Clinical N1 or > 5 pathologic N1 with all involved lymph nodes < 3 cm in largest dimension^a Multifocal papillary microcarcinoma with ETE and <i>BRAF</i>^{V600E} mutated (if known)^a
ATA high risk	Macroscopic invasion of tumor into the perithyroidal soft tissues (gross ETE) Incomplete tumor resection Distant metastases Postoperative serum thyroglobulin suggestive of distant metastases Pathologic N1 with any metastatic lymph node ≥ 3 cm in largest dimension^a Follicular thyroid cancer with extensive vascular invasion (> 4 foci of vascular invasion)^a

ATA – Yüksek Risk Grubu

- Peri-tiroidal dokuya makroskopik tümör invazyonu
- İnkomplet tümör rezeksiyonu
- Uzak metastaz
- Postoperatif dönemde uzak metastaz düşündüren yüksek serum Tg düzeyleri
- 3 cm ve daha büyük metastatik lenf nodu içeren N1 hastalık
- Yaygın vasküler invazyon gösteren folliküler karsinom

Guidelines for radioiodine therapy of differentiated thyroid cancer

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-008-0883-1

A. Definite indications

1. Unresectable iodine-avid lymph node metastases where one or more of the following is true:
 - morphological imaging does not reveal location
 - surgery is high-risk or contraindicated
 - distant involvement is present that would indicate RAIT anyways
2. Iodine-avid pulmonary micrometastases, especially before they become visible on CT
3. Non-resectable or partially resectable iodine-avid pulmonary macrometastases
4. Non-resectable or partially resectable iodine-avid soft tissue metastases

Guidelines for radioiodine therapy of differentiated thyroid cancer

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- Kür veya palyasyon amacıyla I-131 kullanımında
 - Operabilite
 - İyot tutma potansiyeli
 - Hastalık lokalizasyonu
 - Lenf nodu, akciğer, yumuşak doku
 - Kemik ve beyin
 - Tümör özellikleri
 - Stabil hastalık
 - Yaş
 - Genel sağlık durumu
 - I-131'e bağlı potansiyel riskler

Yüksek Risk Grubunda I-131 Kullanımı

- Metastatik papiller ve folliküler karsinomda sürvi avantajı
- Rutin öneri – yüksek doz

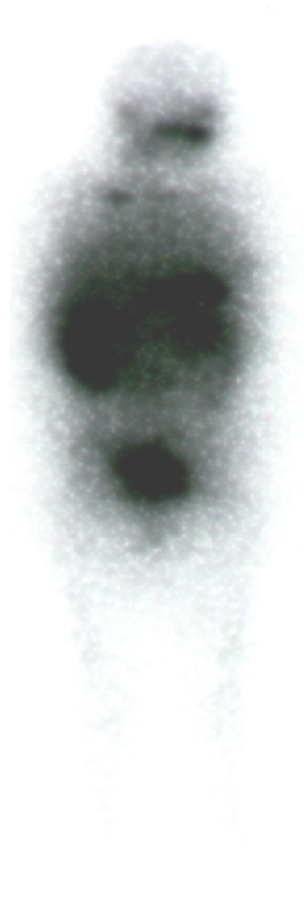
I-131 Tedavisi



200 mCi (1994)



400 mCi (1995)



600 mCi (1996)



800 mCi (1998)

Orta Risk Grubunda I-131 Kullanımı

ADJUVAN TEDAVİ

ATA 2015

[B36] What is the role of RAI (including remnant ablation, adjuvant therapy, or therapy for persistent disease) after thyroidectomy in the primary management of DTC?

(D) RAI adjuvant therapy should be considered after total thyroidectomy in ATA intermediate-risk level DTC patients.

ATA - 2015

TABLE 11. ATA 2009 RISK STRATIFICATION SYSTEM WITH PROPOSED MODIFICATIONS

ATA low risk	Papillary thyroid cancer (with all of the following): • No local or distant metastases; • All macroscopic tumor has been resected • No tumor invasion of loco-regional tissues or structures • The tumor does not have aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma) • If ^{131}I is given, there are no RAI-avid metastatic foci outside the thyroid bed on the first posttreatment whole-body RAI scan • No vascular invasion • Clinical N0 or ≤ 5 pathologic N1 micrometastases (< 0.2 cm in largest dimension)^a Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer^a Intrathyroidal, well differentiated follicular thyroid cancer with capsular invasion and no or minimal (< 4 foci) vascular invasion^a Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including <i>BRAF</i>^{V600E} mutated (if known)^a
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ATA – Orta Risk Grubu

- Peri-tiroidal dokuya mikroskopik invazyon
- İlk RAI tedavisinde boyunda iyot (+) metastatik odak
- Agresif histopatoloji (tall cell, hobnail varyant, kolumnar hücreli)
- Vasküler invazyon gösteren papiller karsinom
- Klinik N1, > 5 patolojik N1, tüm lenf nodları < 3 cm
- Multifokal papiller mikrokarsinom ekstratiroidal uzanım veya BRAF mutasyonu

Guidelines for radioiodine therapy of differentiated thyroid cancer

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-008-0883-1

B. Optional indications

1. Recurrent iodine-avid lymph node or distant metastases, as an adjuvant to surgery
2. Unresectable iodine-avid lymph node metastases where one or more of the following is true:
 - size is small
 - involvement includes numerous nodes or is widespread
3. Non-resectable or partially resectable iodine-avid bone metastases, especially when symptomatic or threatening vital structures
4. Known or suspected metastatic DTC where iodine avidity is not yet known, especially if Tg is detectable or increasing^a
5. Anaplastic or poorly differentiated thyroid carcinomas that have (relevant) well-differentiated areas or express Tg, especially if symptomatic or progressive^b

ATA – Orta Risk Grubu

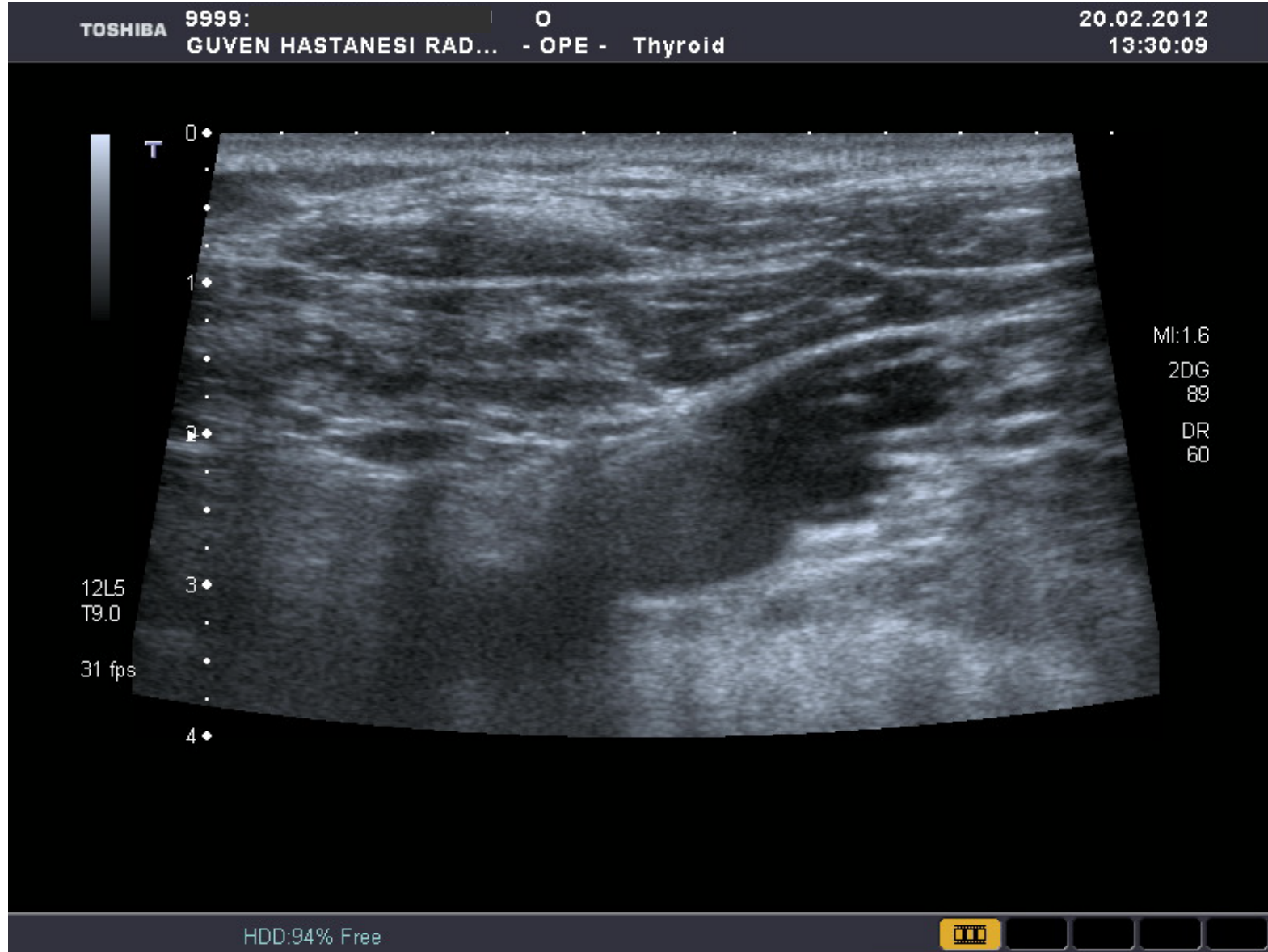
- I-131 kullanımının en önemli gerekçesi
 - Rezidüel nodal hastalık
 - Olası nodal hastalık
- Doz seçimi
 - Ablasyon
 - Adjuvan tedavi

Nodal Hastalık İyot ile Tedavi Olur mu?

(MK)

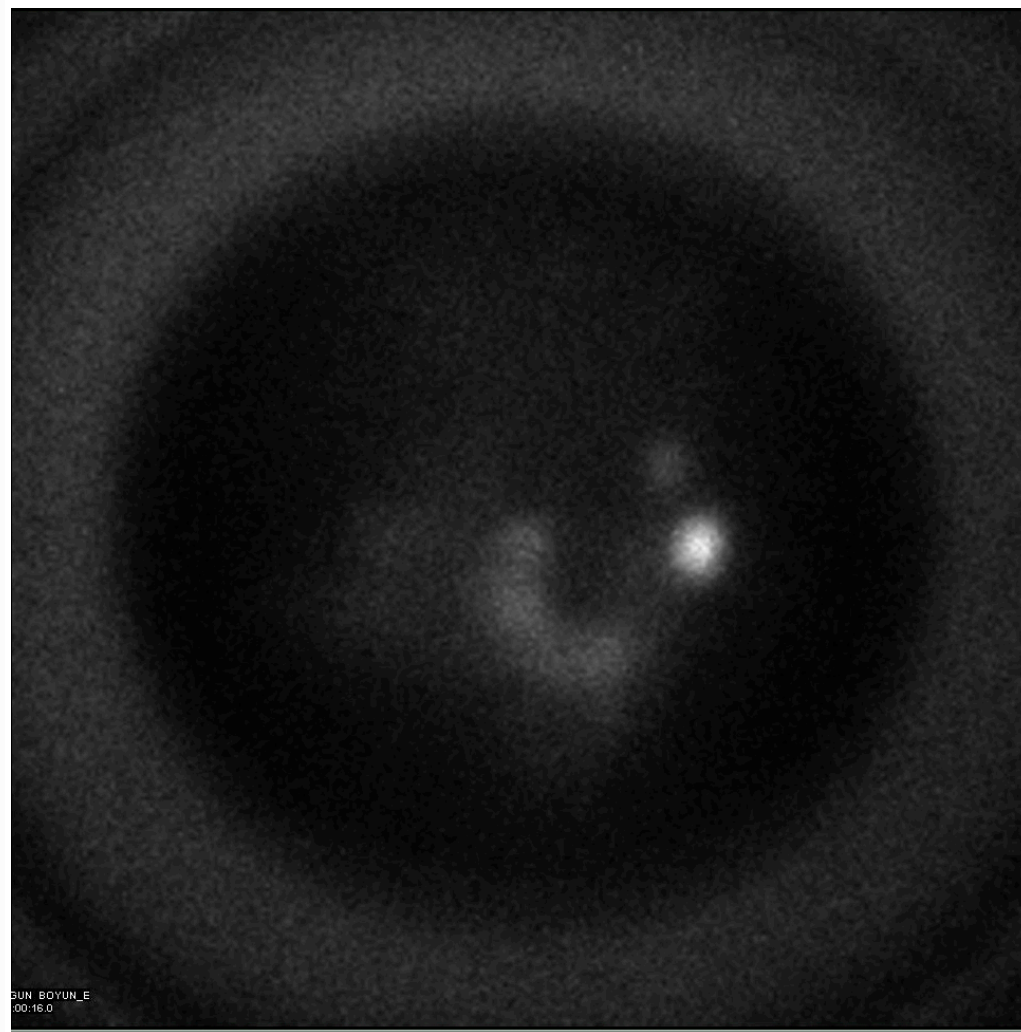
- 59 yaşında erkek hasta
- Preoperatif US nodal metastaz bulgusu yok
- 3 hafta önce total tiroidektomi
- Patoloji klasik tip papiller karsinom
 - Tümör çapı 15 mm,
 - Kapsül invazyonu mevcut
 - Tümör lokalizasyonu belirtilmemiş
- Lenf nodu bilgisi yok

(MK) I-131 öncesi US



(MK)

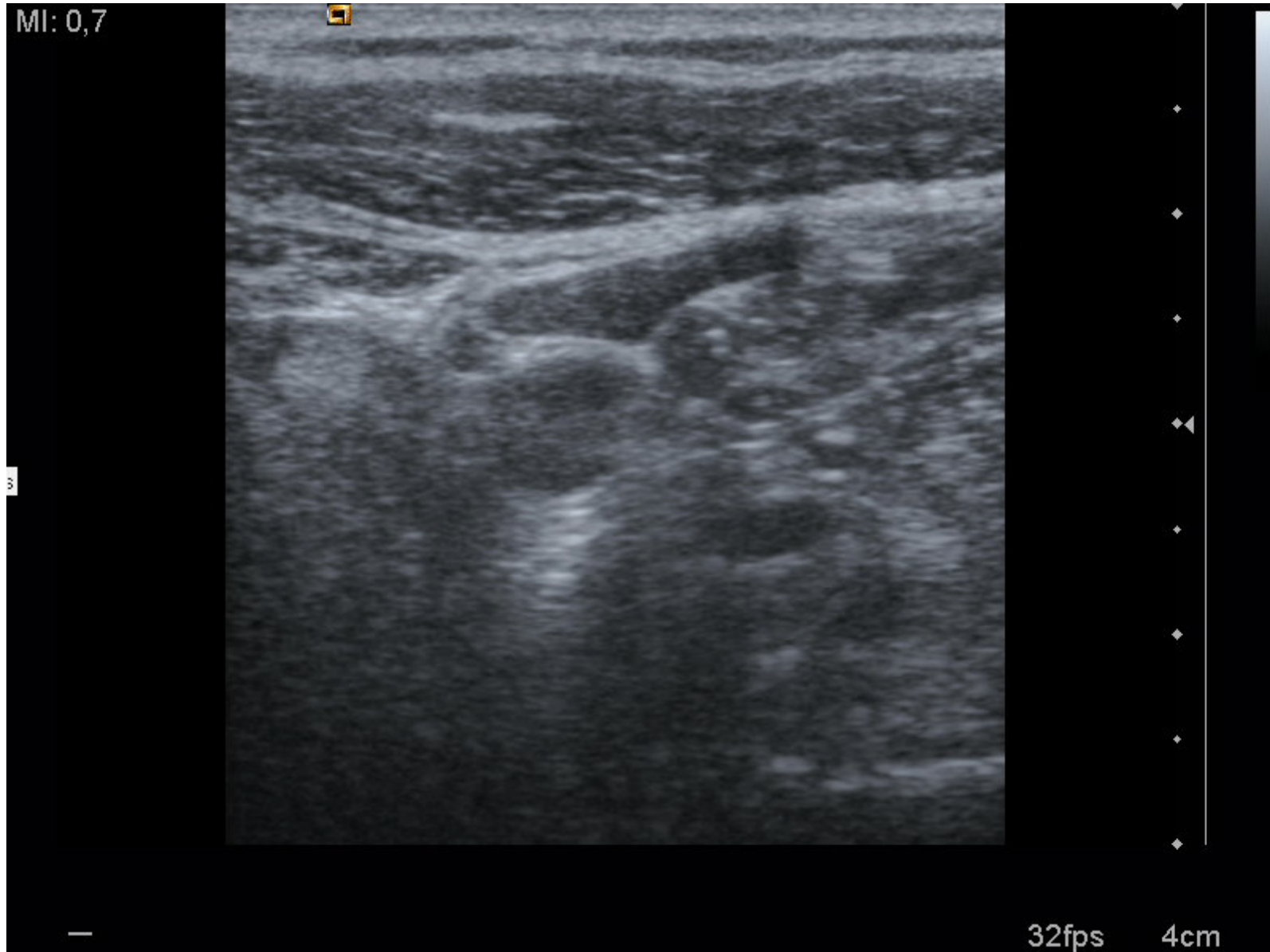
- Sol alt servikalde sınırlı nodal metastaz
- TSH 48.60 μ IU/mL
- Tg 35.49 ng/mL
- Tg-Ab normal
- 100 mCi I-131



(MK) 100 mCi sonrası 7. gün



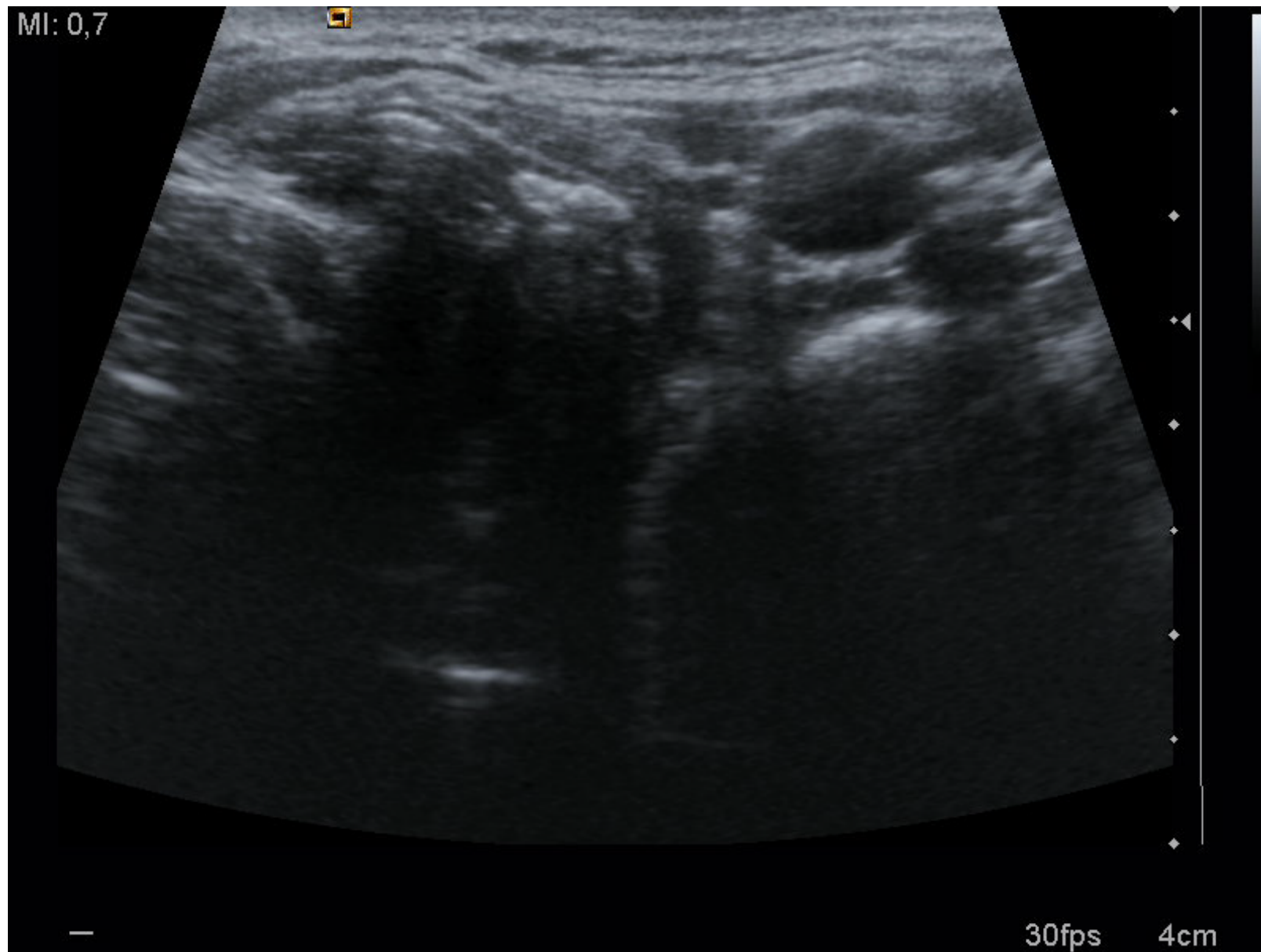
(MK) 100 mCi sonrası 6. yıl – Tg <0.1 ng/mL



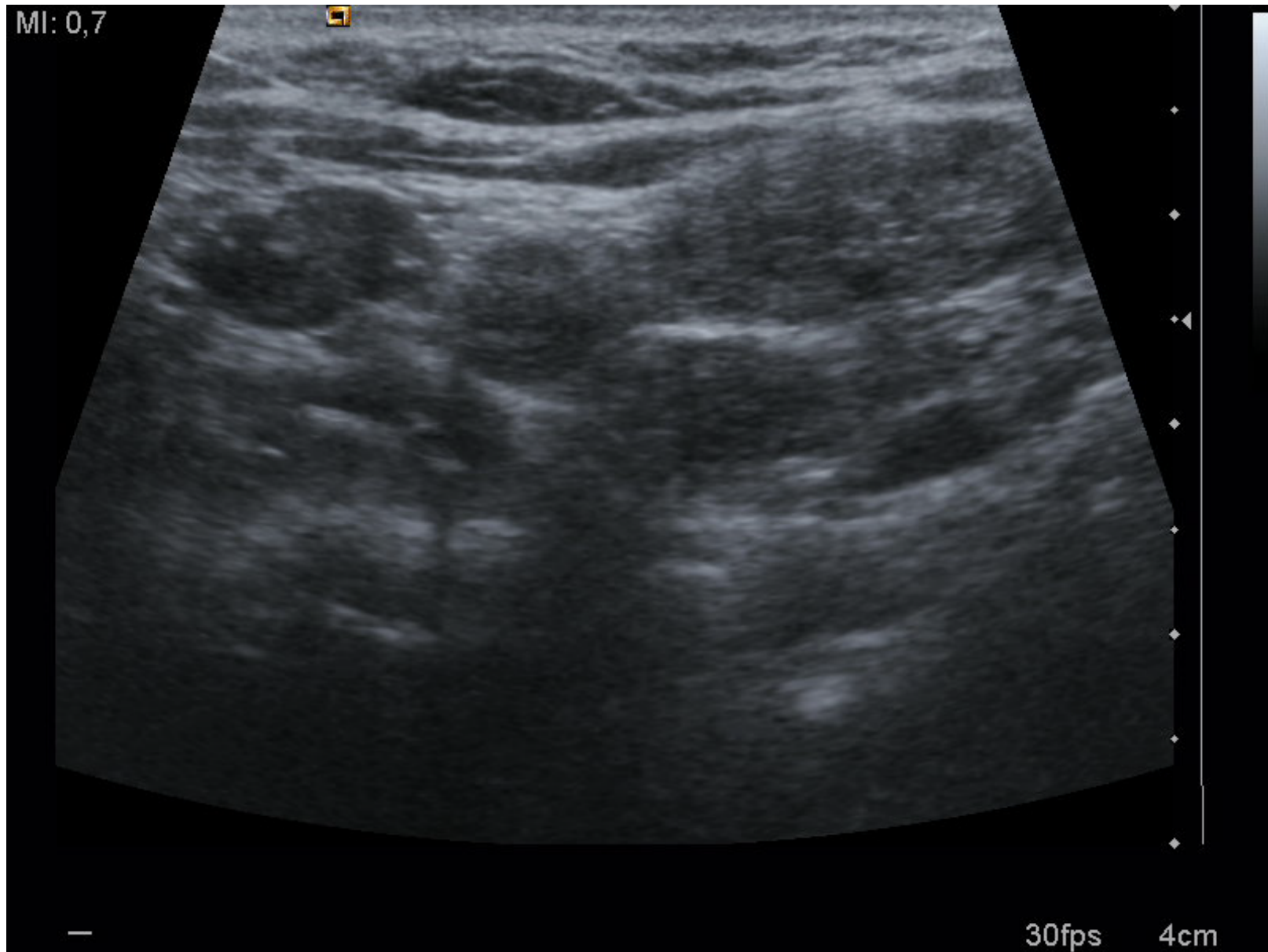
MEK

- 25 yaşında kadın
- Sol lobda yeni tanı papiller karsinom
- Santral ve bilateral servikal metastaz

(MEK) Preoperatif US



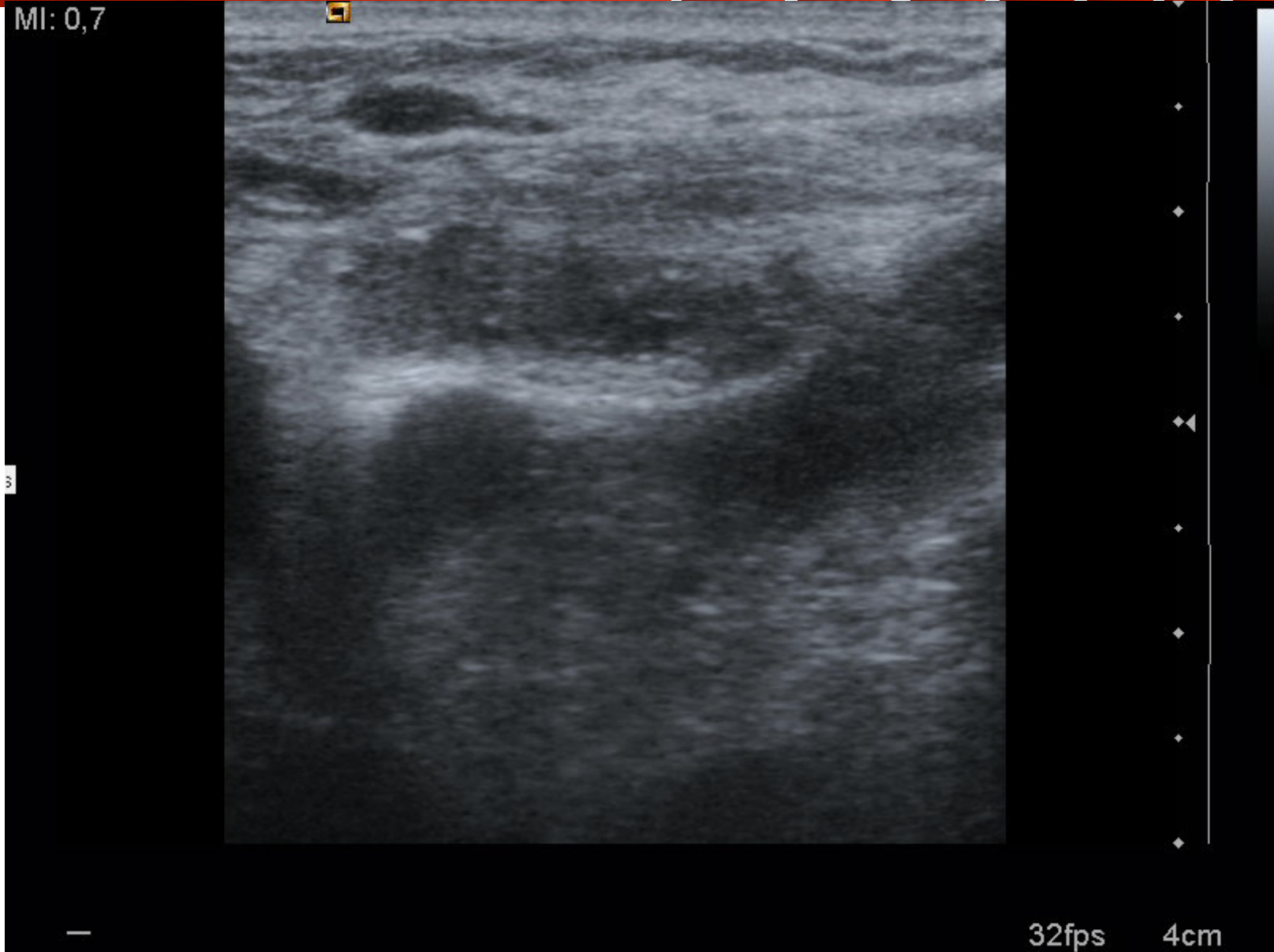
(MEK) Preoperatif US



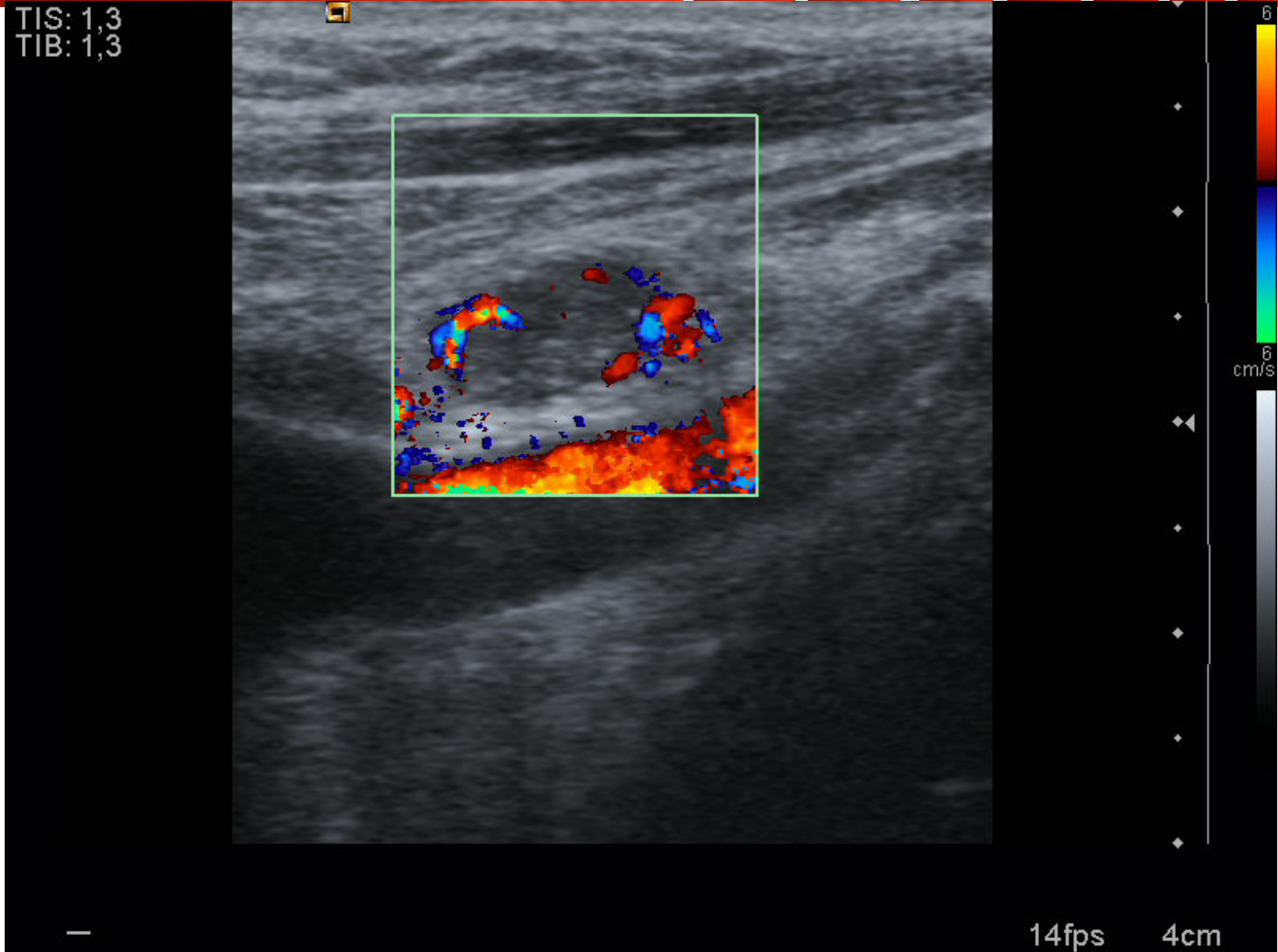
MEK

- Sol lobda 12 mm klasik tip papiller karsinom
- 12/48 nodal metastaz
 - 7 santral
 - 3 sol servikal
 - 2 sağ servikal
- En büyük metastatik nod 5 cm, tümü metastatik

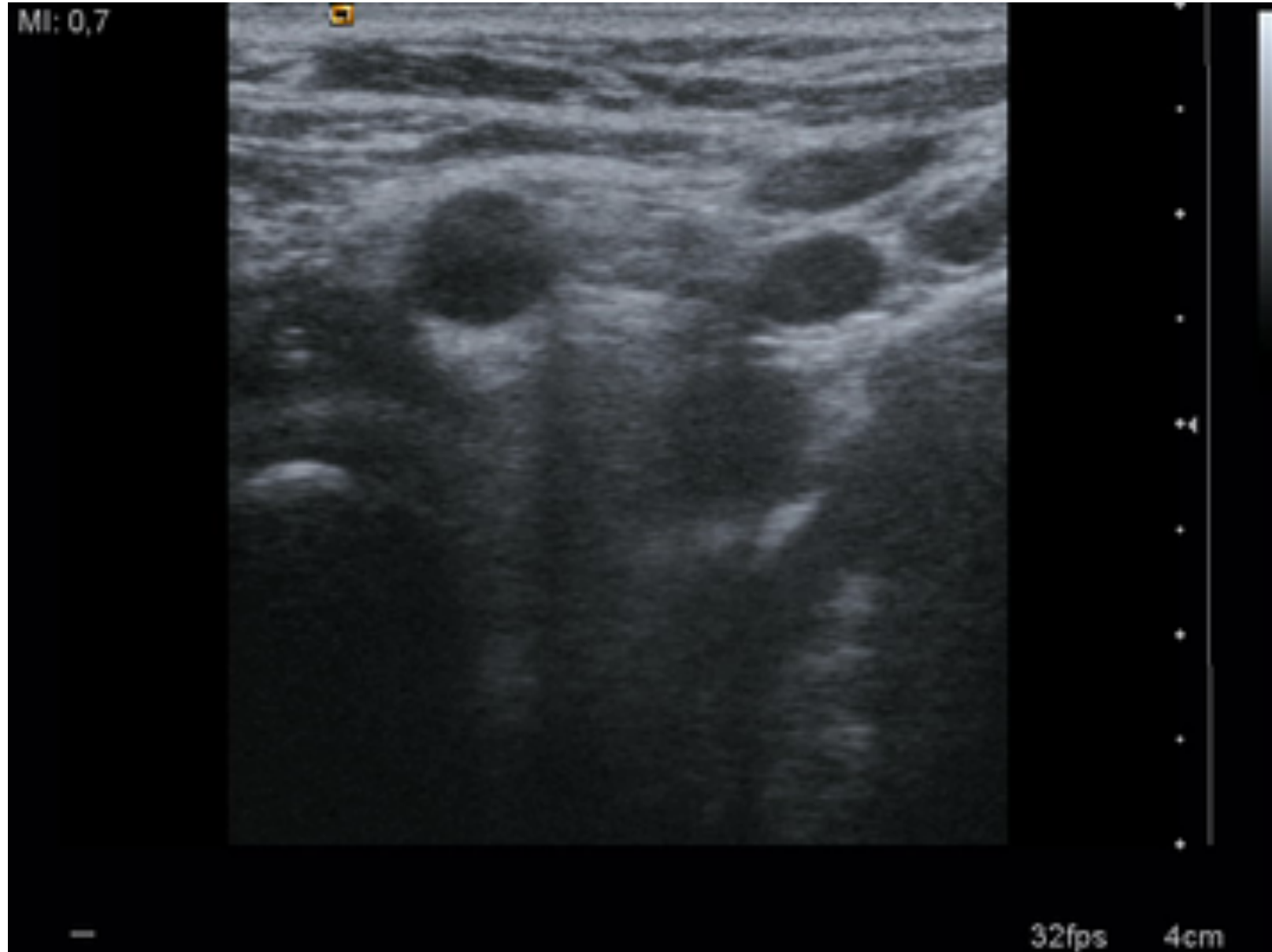
(MEK) 150 mCi I-131 sonrası 10. gün
Tg 82.21 ng/mL, TSH >100 μ IU/mL



(MEK) 150 mCi I-131 sonrası 10. gün
Tg 82.21 ng/mL, TSH >100 µIU/mL



**(MEK) 150 mCi I-131 sonrası 6. ay
İzlemde 4. yıl, US normal, Tg <0.1 ng/mL**



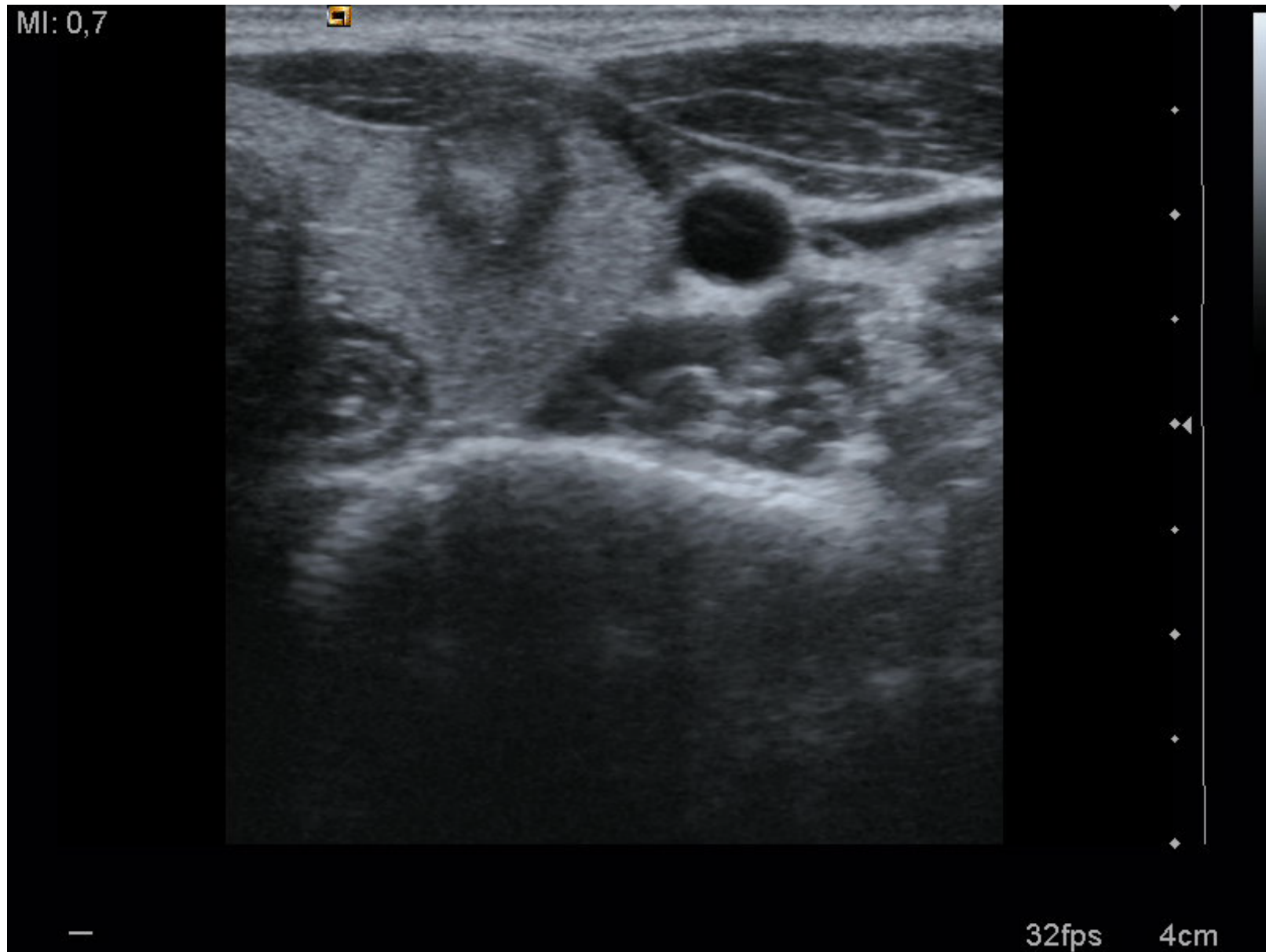
(BE)

- 31 yaşında kadın
- Postoperatif 6. hafta
 - TSH 116 μ IU/mL,
 - Tg 11.1 ng/mL
 - Anti-Tg negatif
- 150 mCi I-131 tedavisi
- Tedavi sonrası supresyon altında Tg 0.7 ng/mL

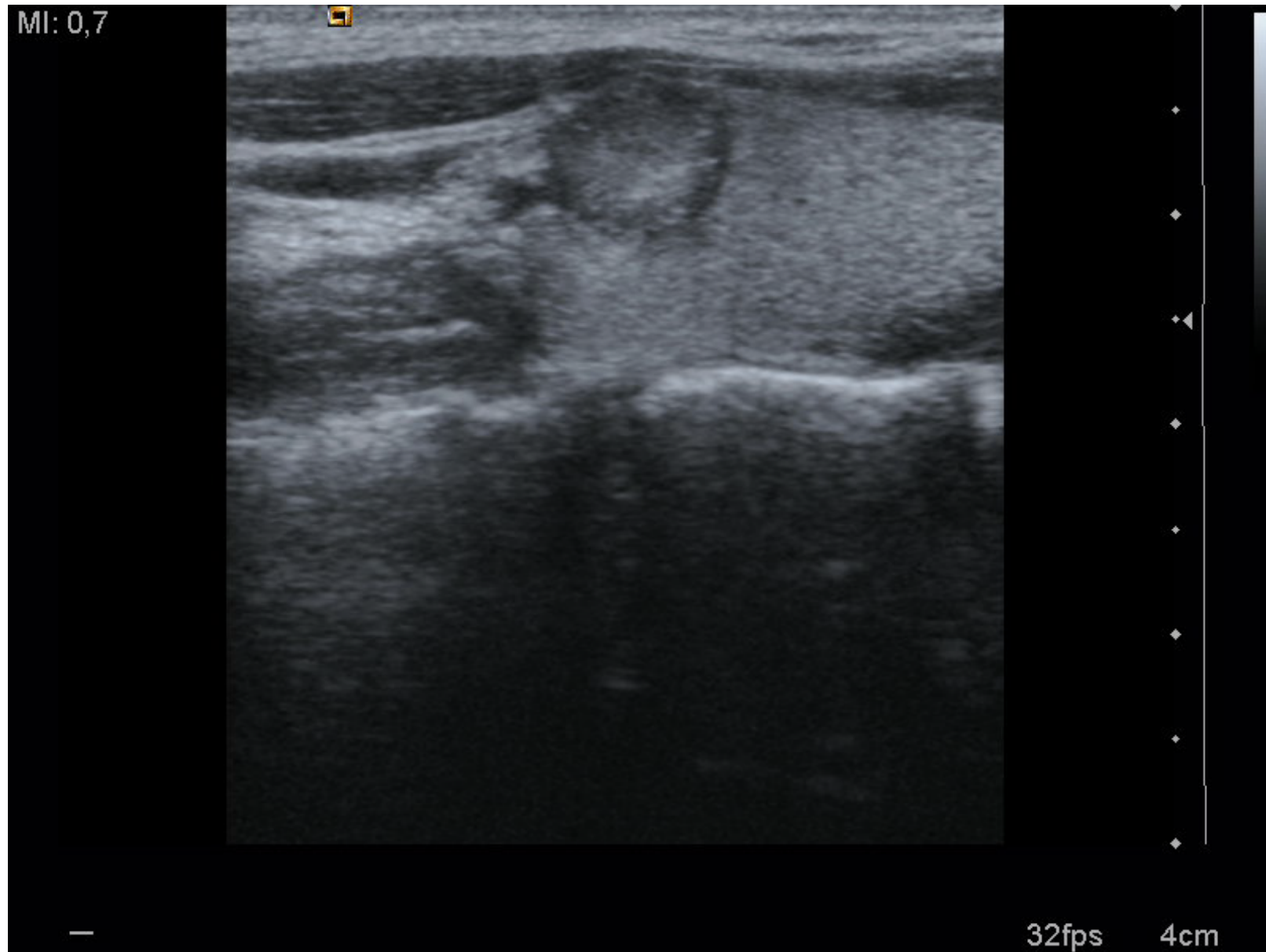
(BE)

- 31 yaşında kadın
- Sol lobda 1 cm folliküler tip papiller karsinom
- Boyalı cerrahi sınır pozitif
- 4/7 metastatik santral lenf nodu
- En büyük nod 3.5 cm, tamamı metastatik, kapsül dışı yayılım pozitif

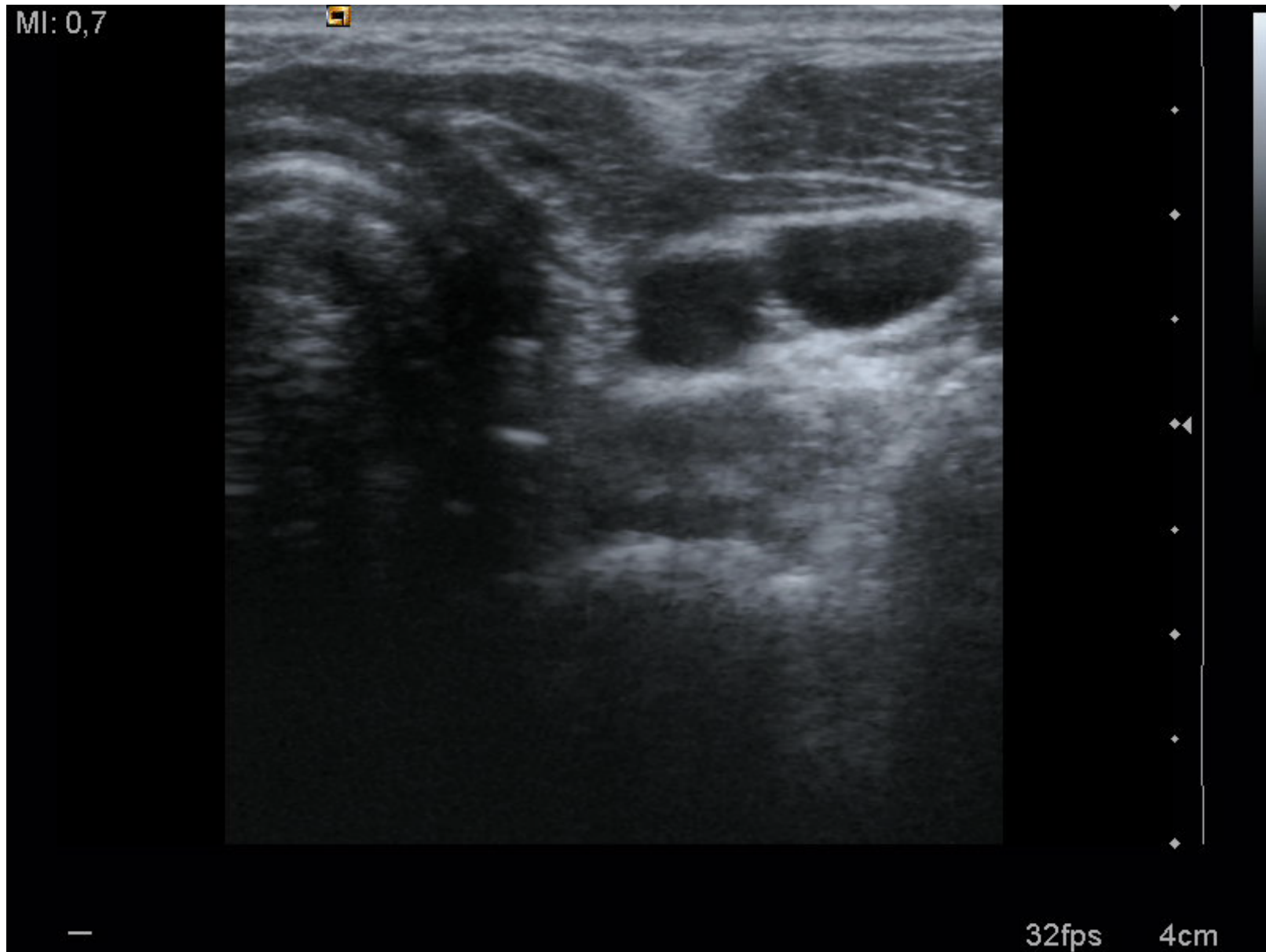
(BE) Preop US



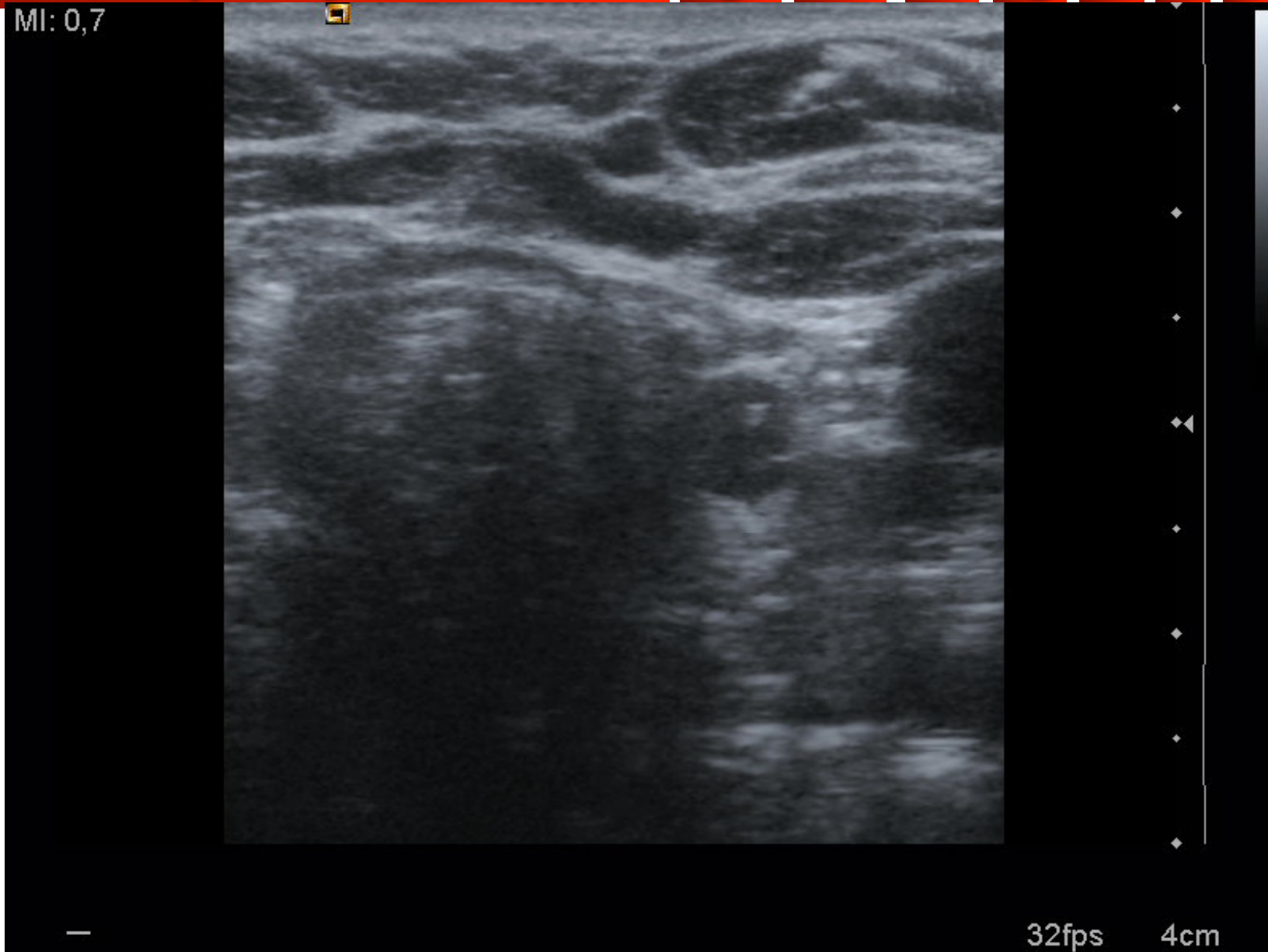
(BE) Preop US



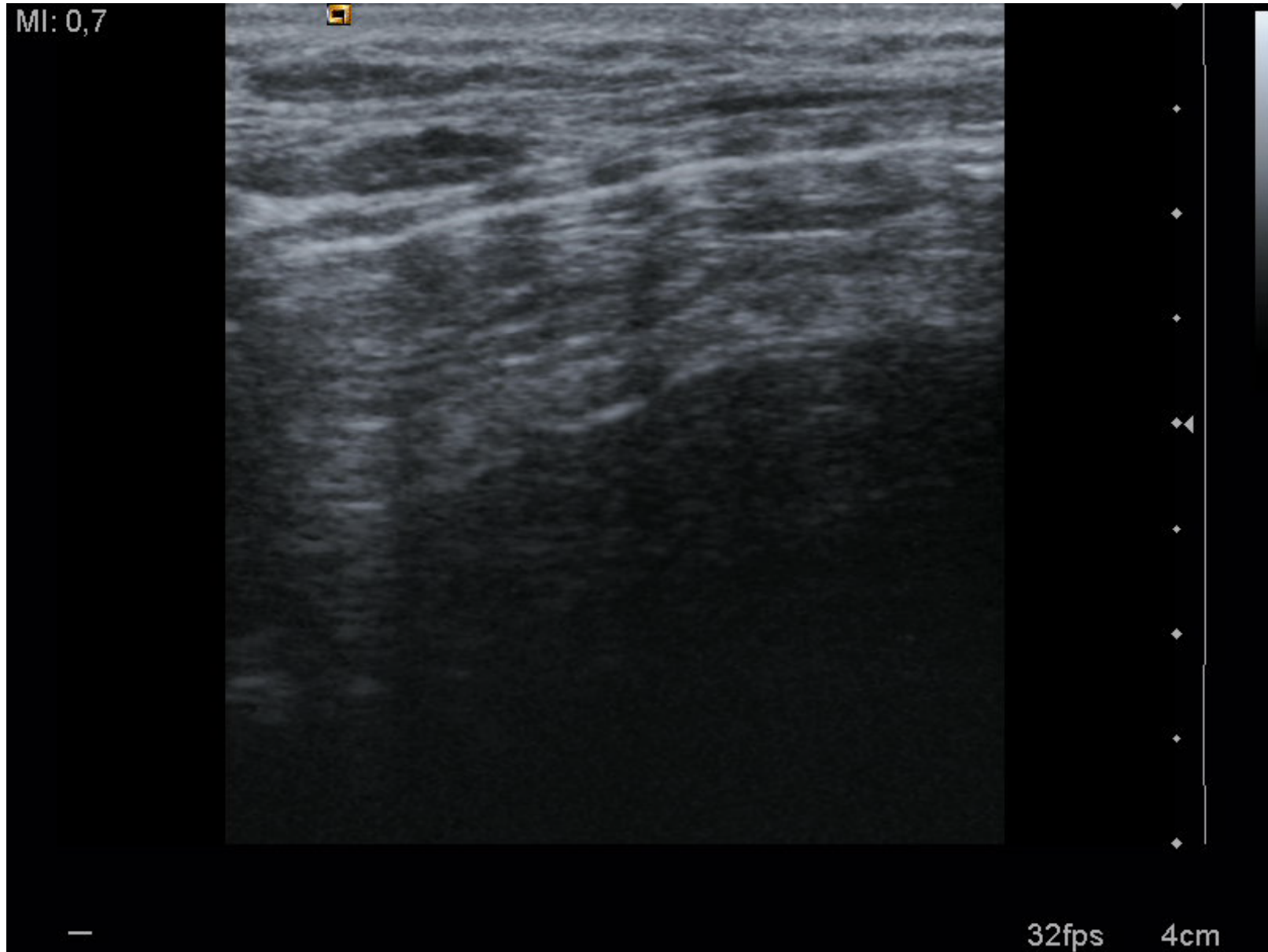
(BE) Postoperatif 1. ay



(BE) 150 mCi I-131 sonrası 6. ay
Supresyon altında Tg 0.6-1.1 ng/mL



(BE) 150 mCi I-131 sonrası 6. ay



(BE)

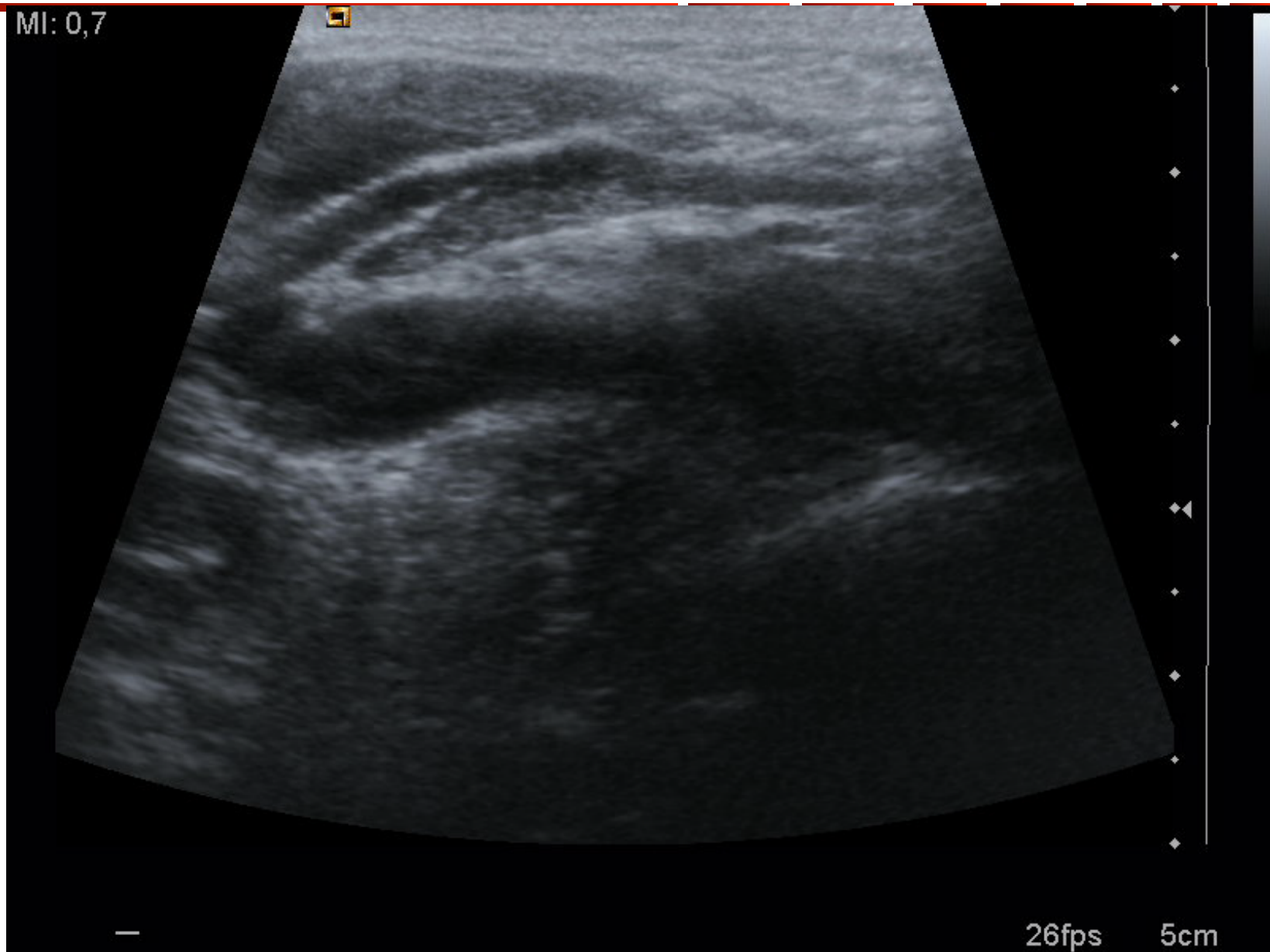
- 1 yıl sonra ROLL eşliğinde sınırlı santral lenf nodu diseksiyonu
- Papiller karsinom metastazı, lenf nodu çapı 8 mm, tamamı metastatik
- Postop suprese Tg <0.1 ng/mL, ek tedavi verilmeden izlemde
- 4 yıllık takipte Tg <0.1 ng/mL ve US normal

(VK)

- 44 yaşında erkek hasta
- Sağ lobda yeni tanı papiller karsinom
- Preoperatif US'de kontralateral nodal metastaz şüphesi
 - İİAB papiller karsinom
 - Tg yıkama negatif

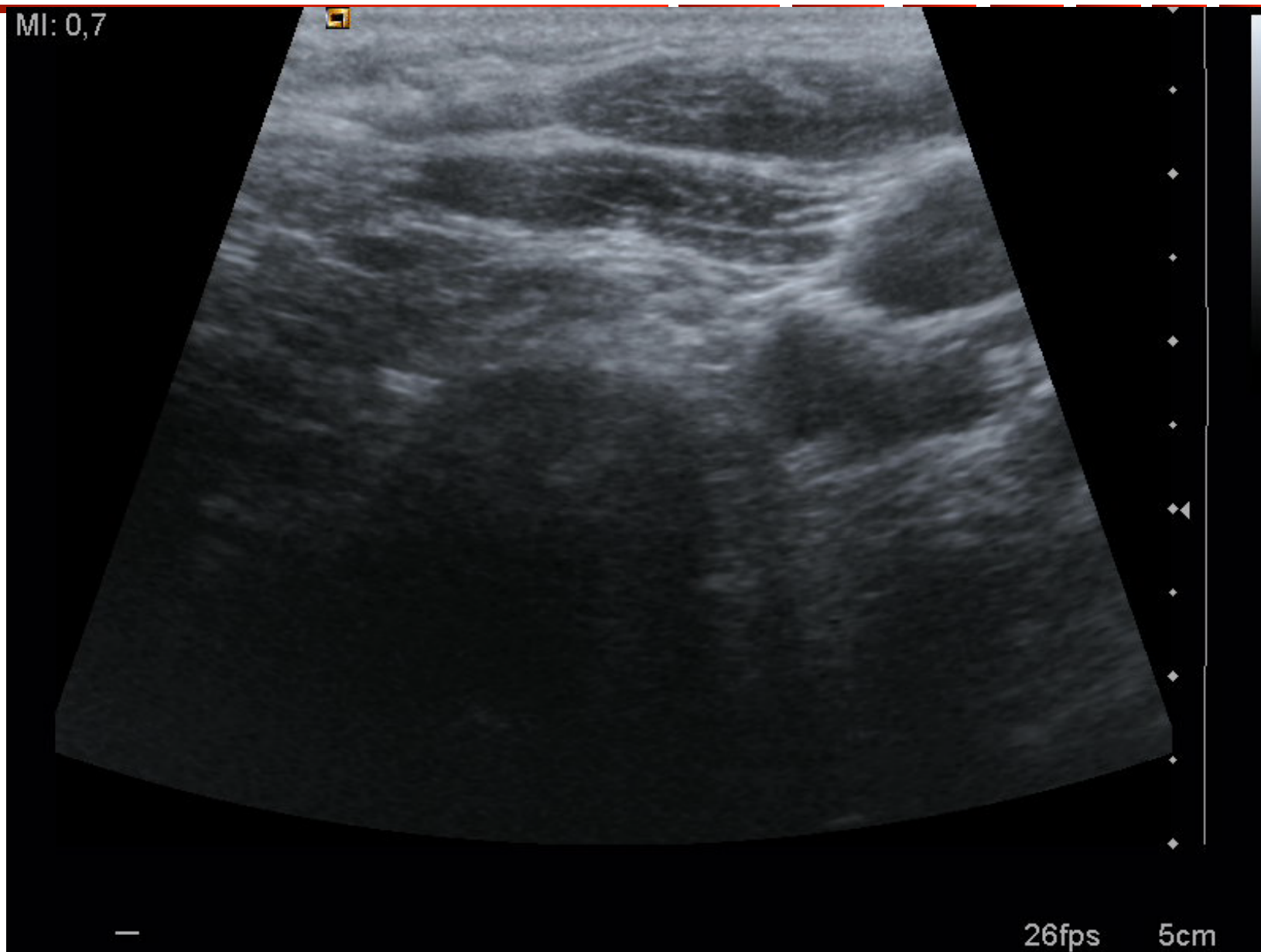
(VK)

MI: 0,7



(VK)

MI: 0,7



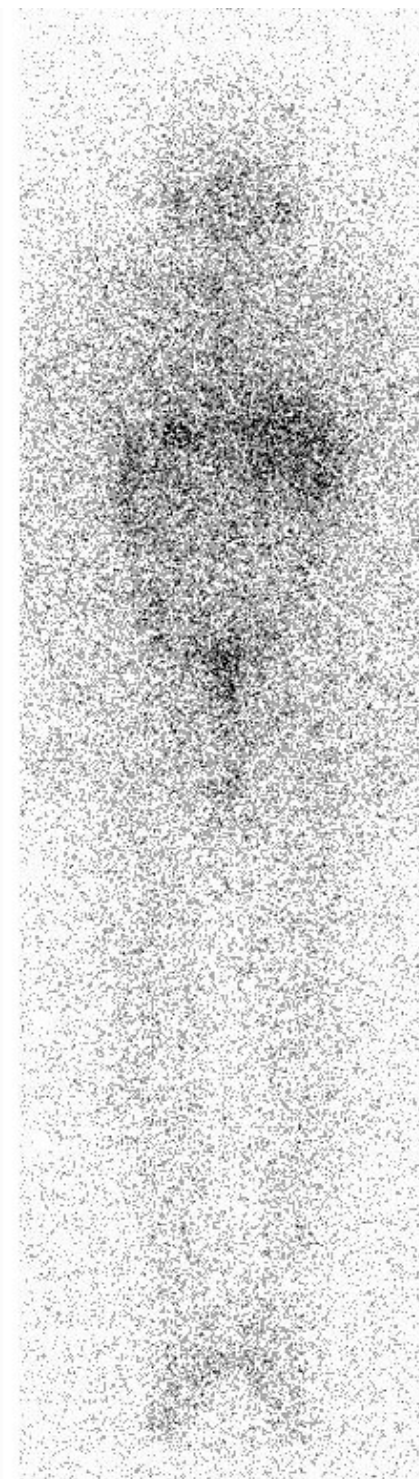
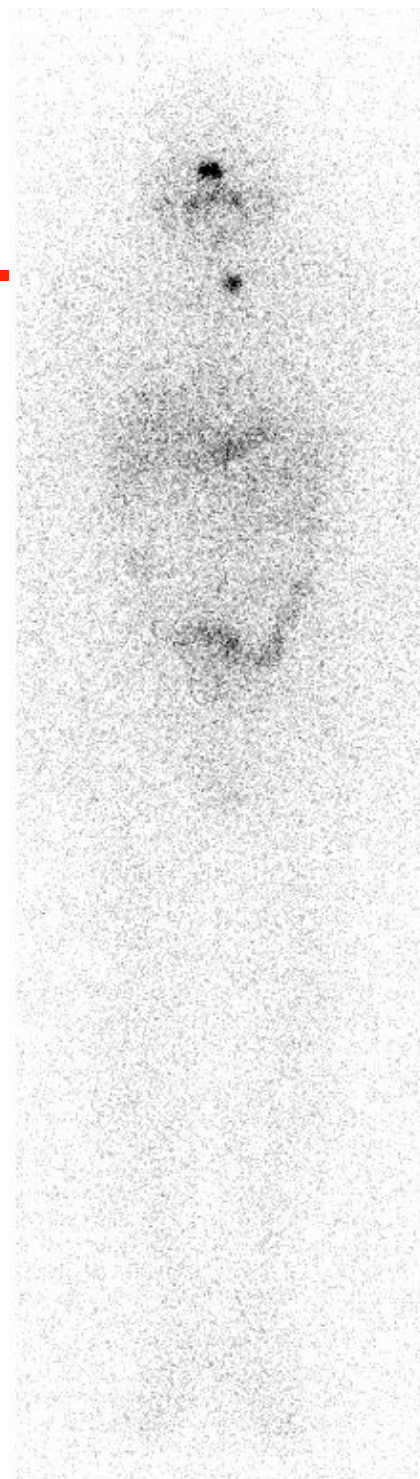
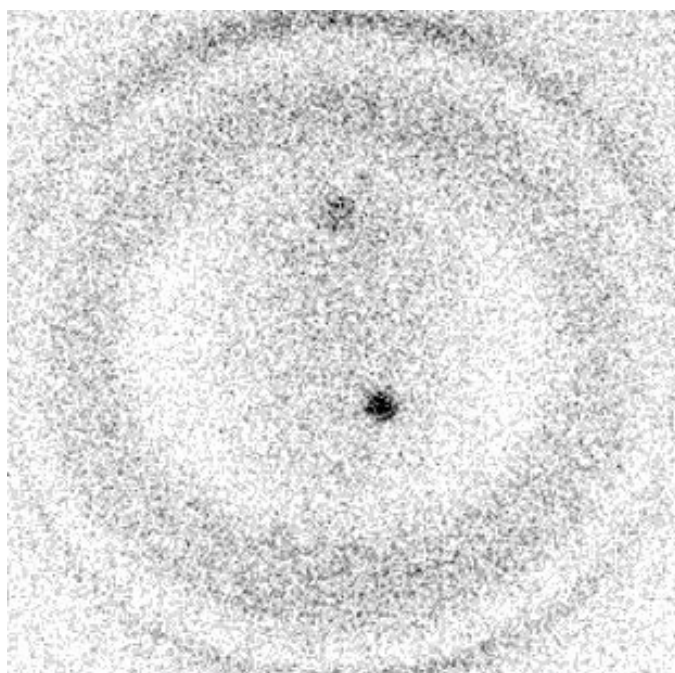
(VK)



(VK)

- Total tiroidektomi + santral ve sol servikal nodal metastaz
- Sağ lobda 6 cm papiller karsinom
- 8/22 sol lateral servikal metastaz
- 0/6 santral lenf nodu
- Postop 6. hafta
 - TSH 88.67 μ IU/mL
 - Tg 0.802 ng/mL
- 30 mCi I-131 ablasyon
- 4. yıl, supresyon altında Tg <0.1 ng/mL, US normal

(VK) 30 mCi

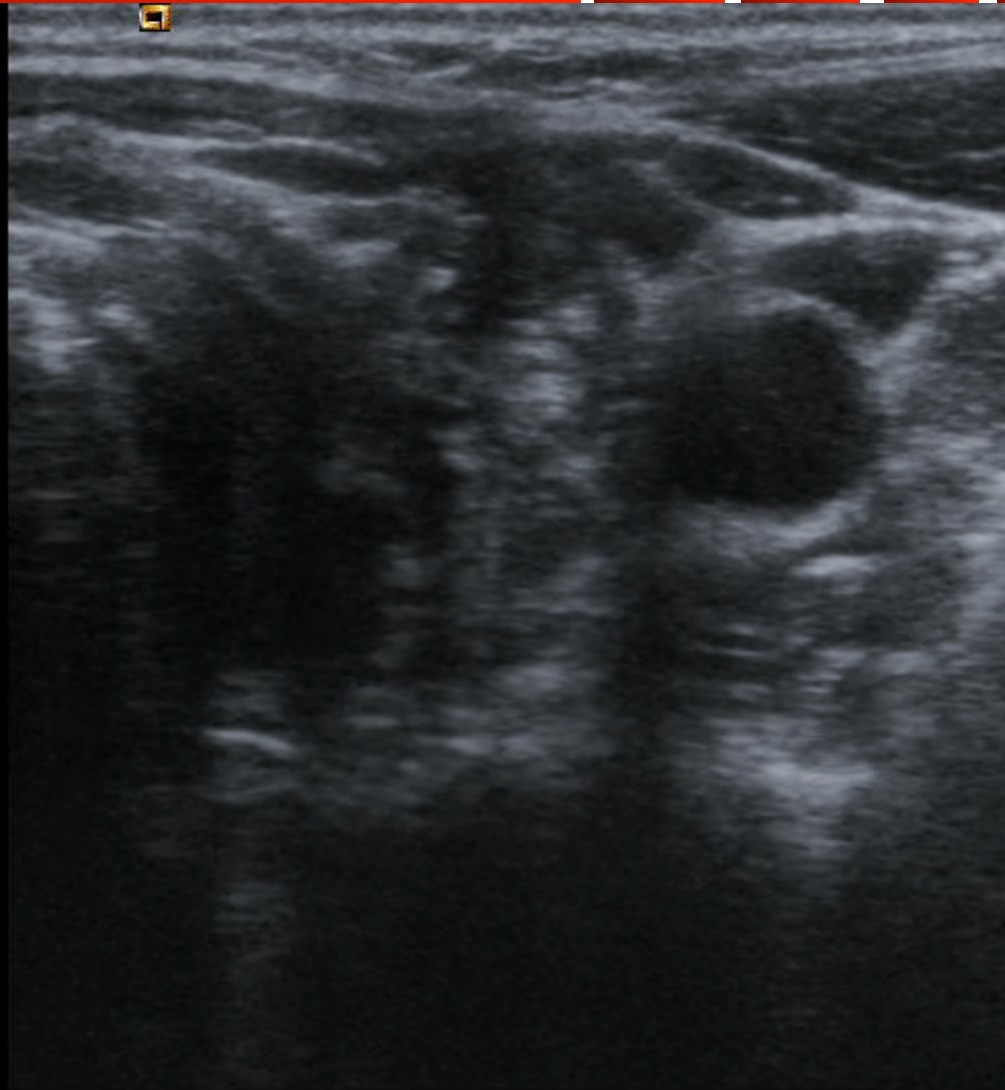


(EÇY)

- 28 yaşında kadın
- Boyunda şişlik
- Tiroidit zemininde sol lobda papiller karsinom, sol servikal ve santral kompartmanda metastatik lenf nodları

(EÇY)

MI: 0,7

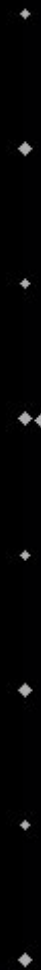
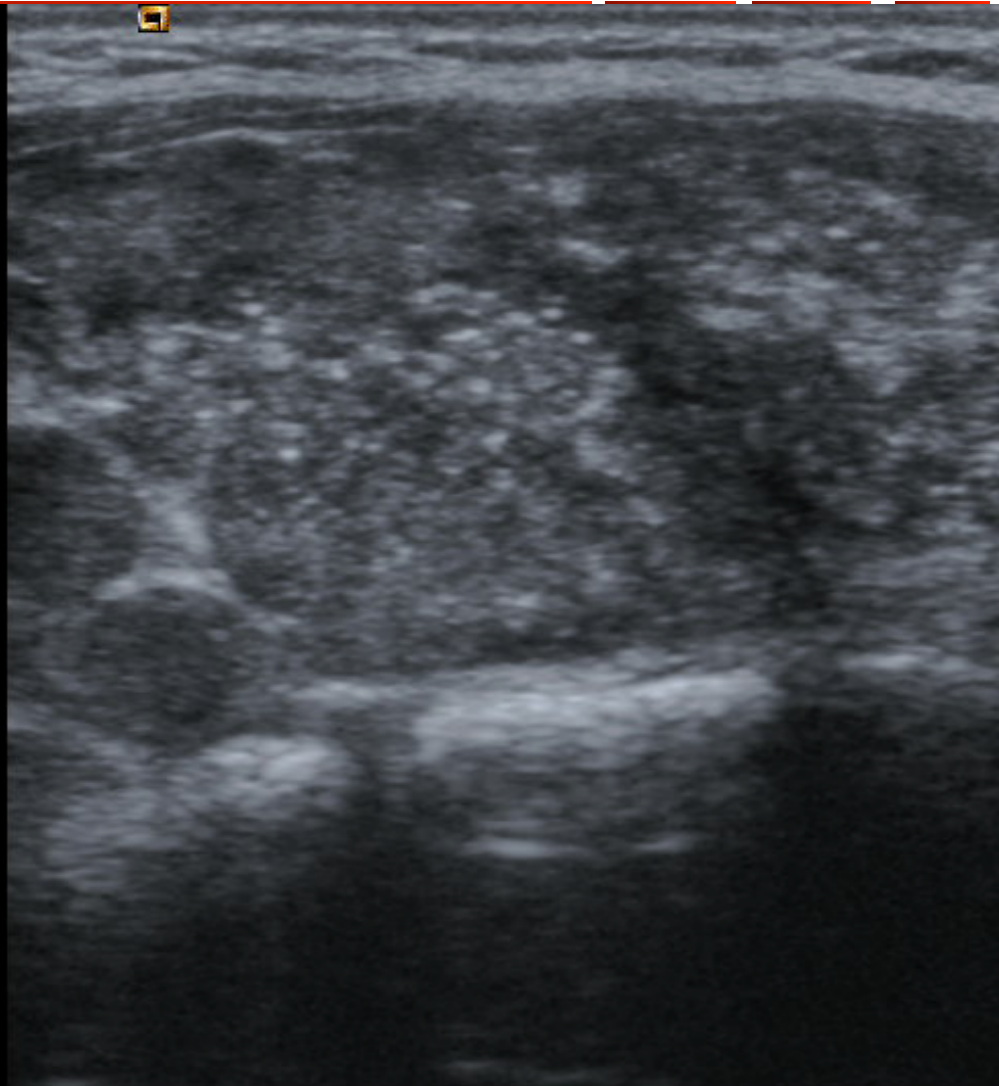


32fps

4cm

(EÇY)

MI: 0,7

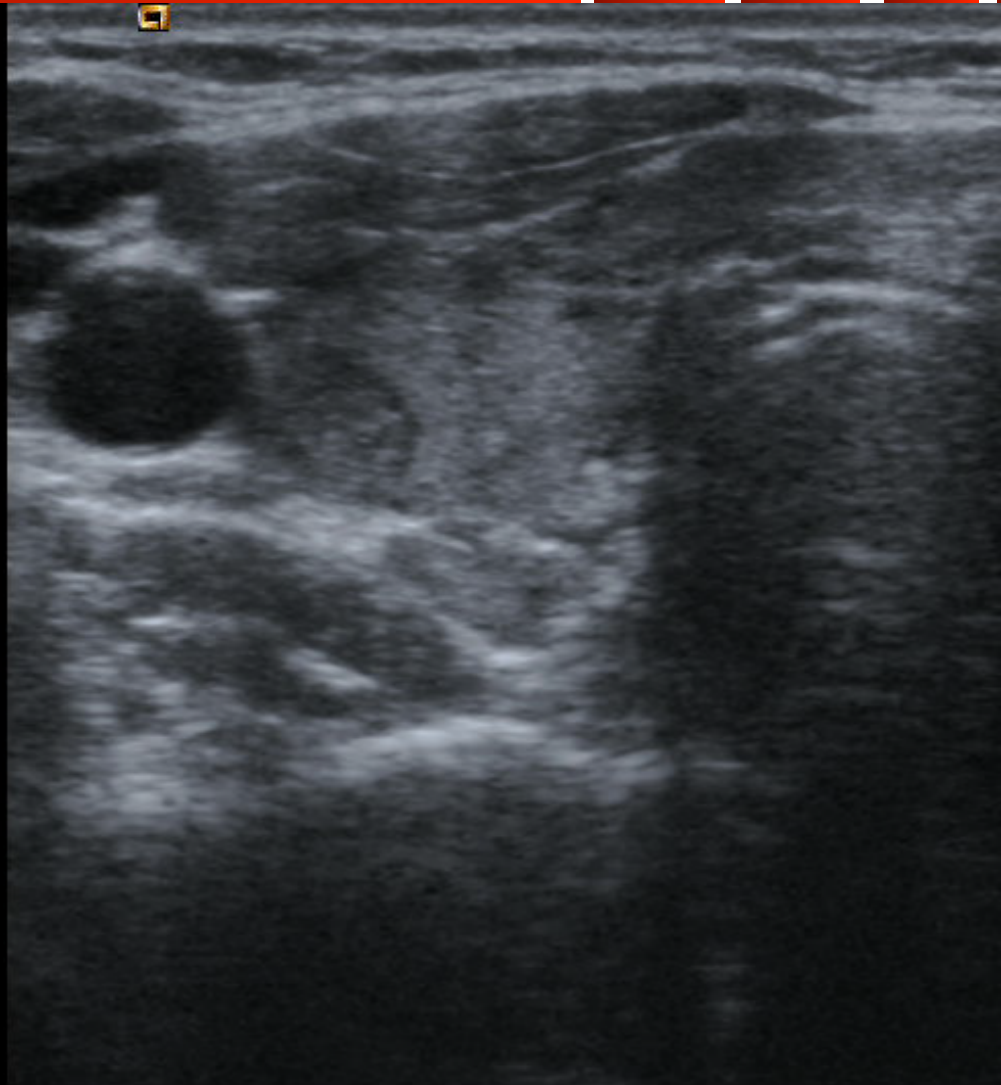


32fps

4cm

(EÇY)

MI: 0,7

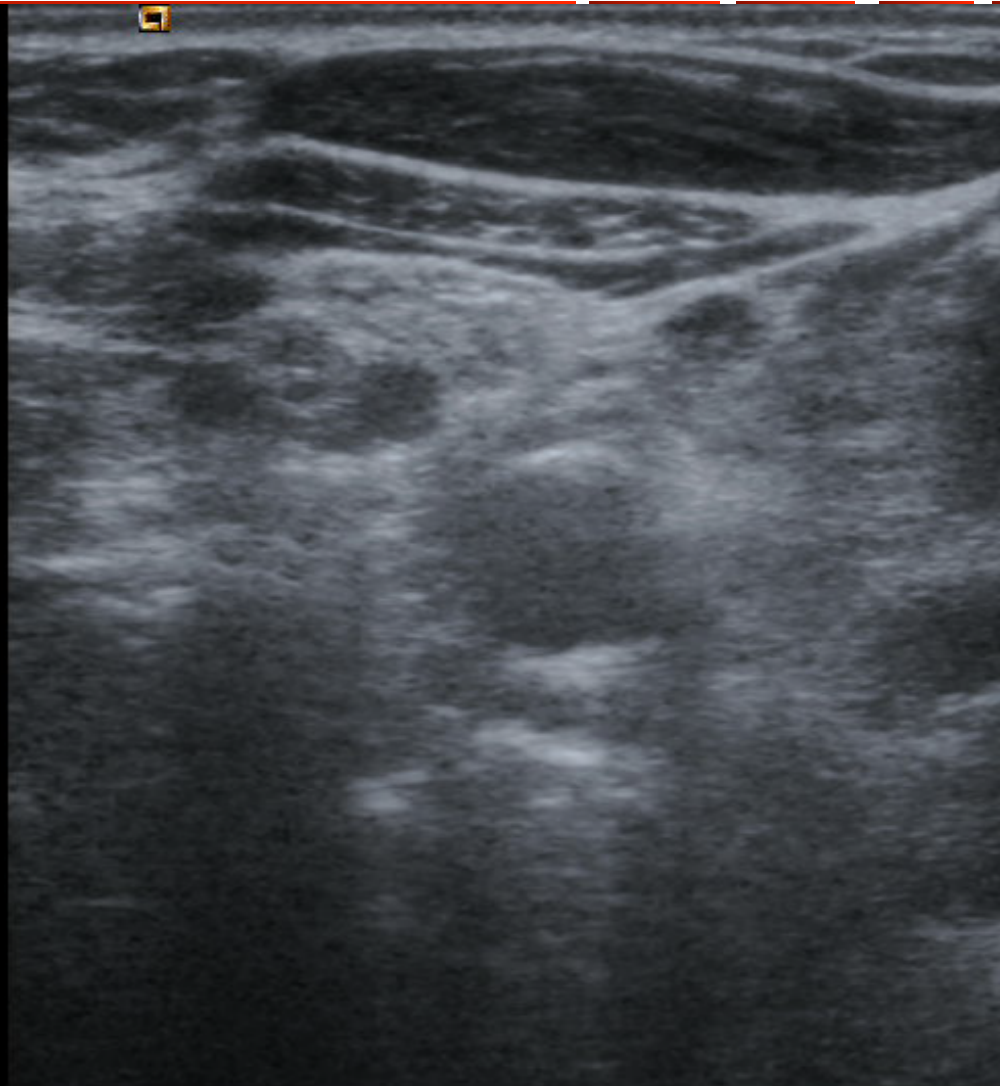


32fps

4cm

(EÇY)

MI: 0,7

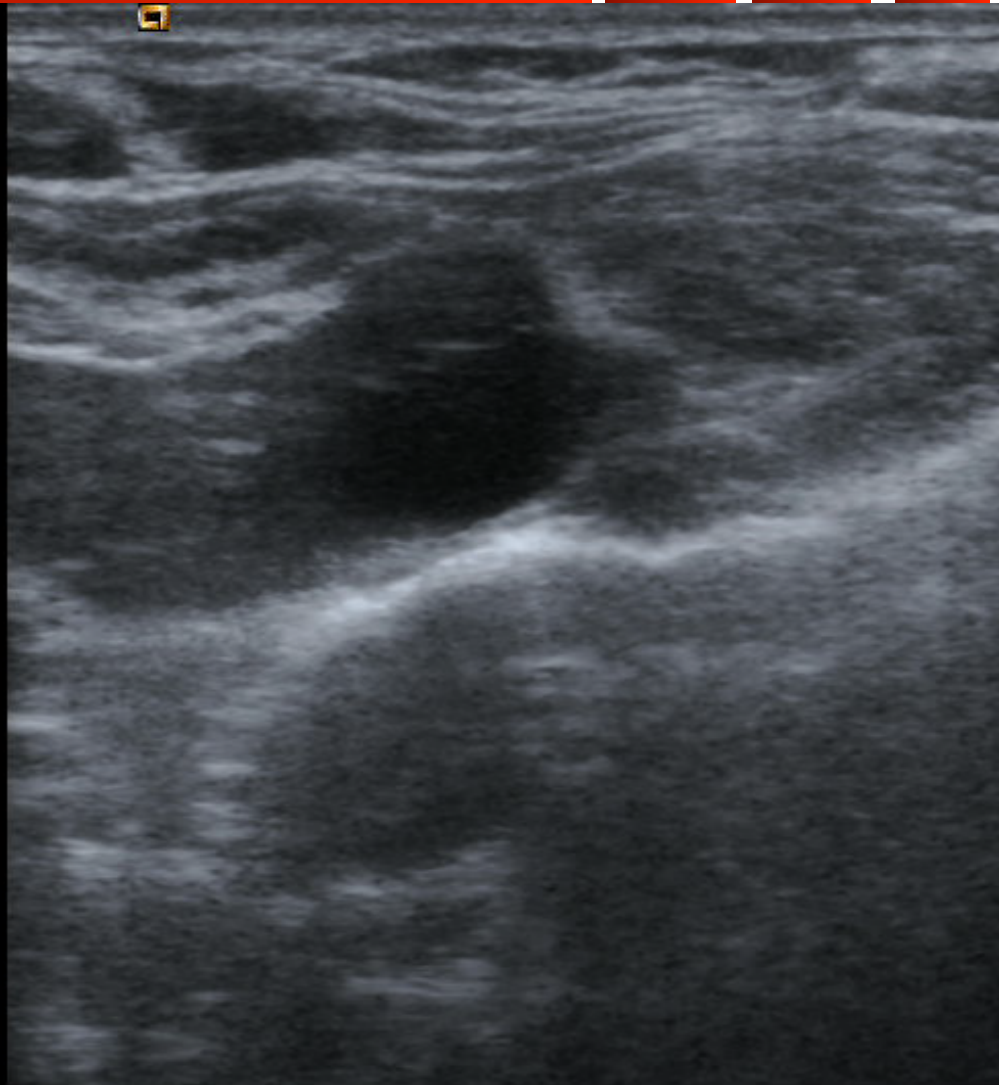


32fps

4cm

(EÇY)

MI: 0,7



32fps

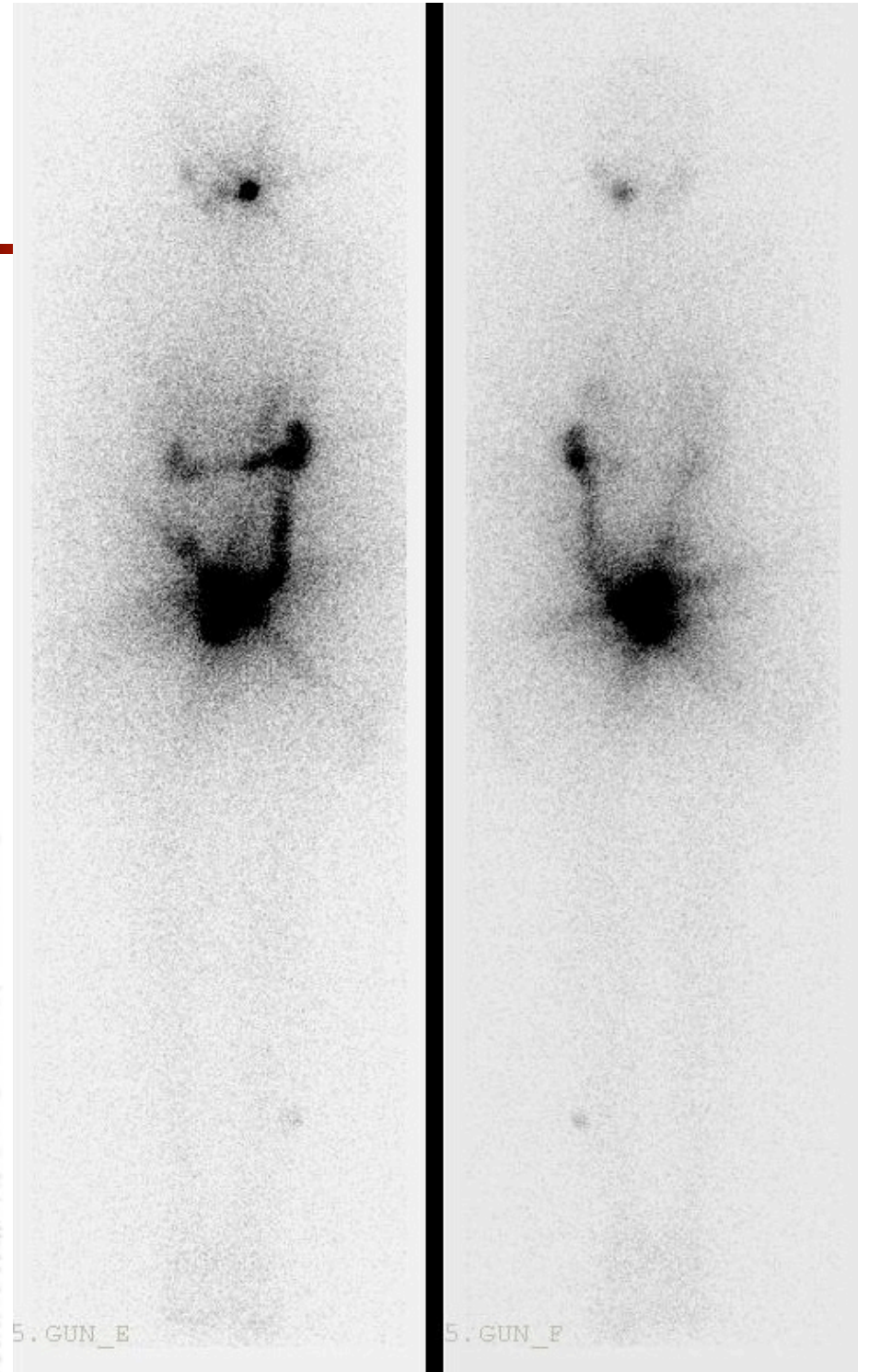
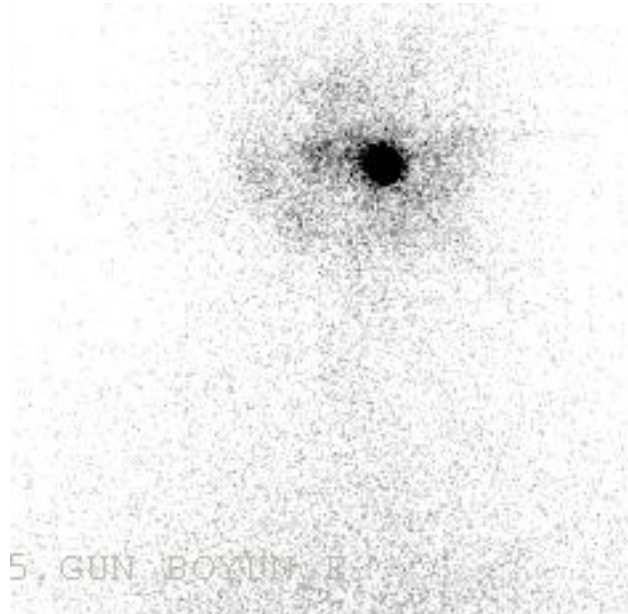
4cm

(EÇY)

- Sol lobda 16 mm papiller karsinom, kribriform morular
- LVI var
- Tümör dışı dokuda kronik lenfositik tiroidit
- 12/18 metastatik sol lateral servikal metastaz
 - 12 mm $\frac{3}{4}$ 'ü metastatik
- 19/41 metastatik sol lateral lenf nodu
 - 25 mm tümü metastatik, kapsül dışı yayılım yok

(EÇY) 150 mCi I-131

- Stimüle Tg ve postop US yok
- TSH >100 μ IU/mL,
- Tg <0.1 ng/mL,
- Tg-Ab normal,
- Boyun US normal
- 6. ay sialoadenit

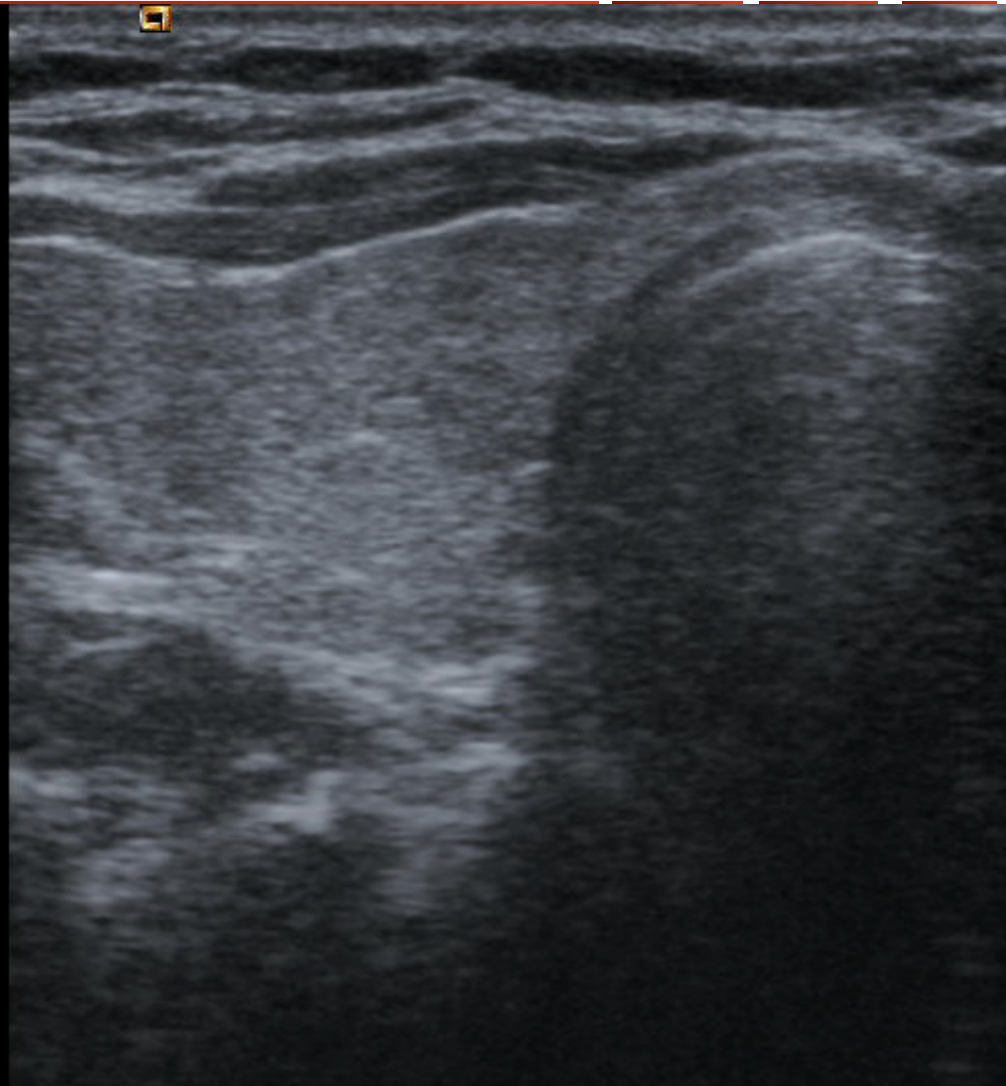


(SS)

- 46 yaşında erkek
- Sağ lobdan İİAB papiller karsinom
- US'de patolojik lenf nodu tanımlanmamış

(SS)

MI: 0,7



32fps

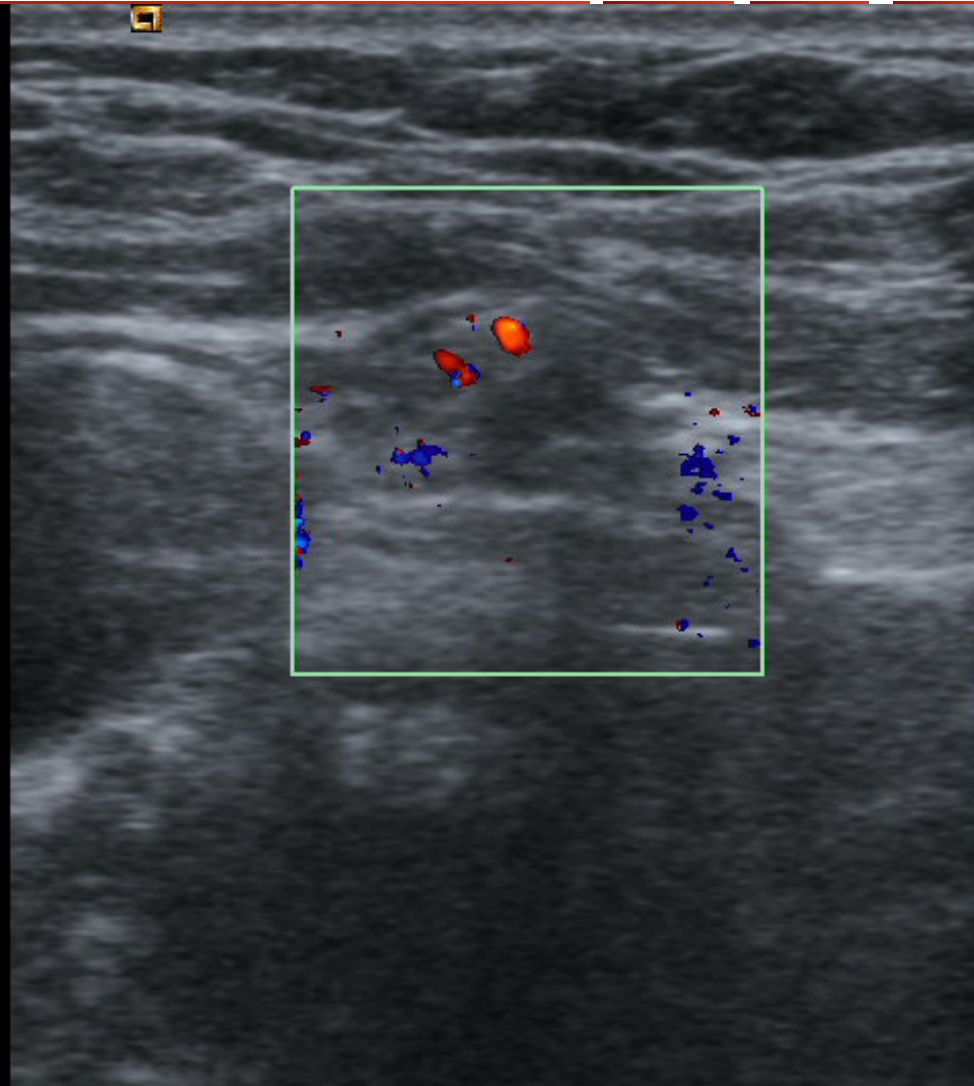
4cm

(SS)



(SS)

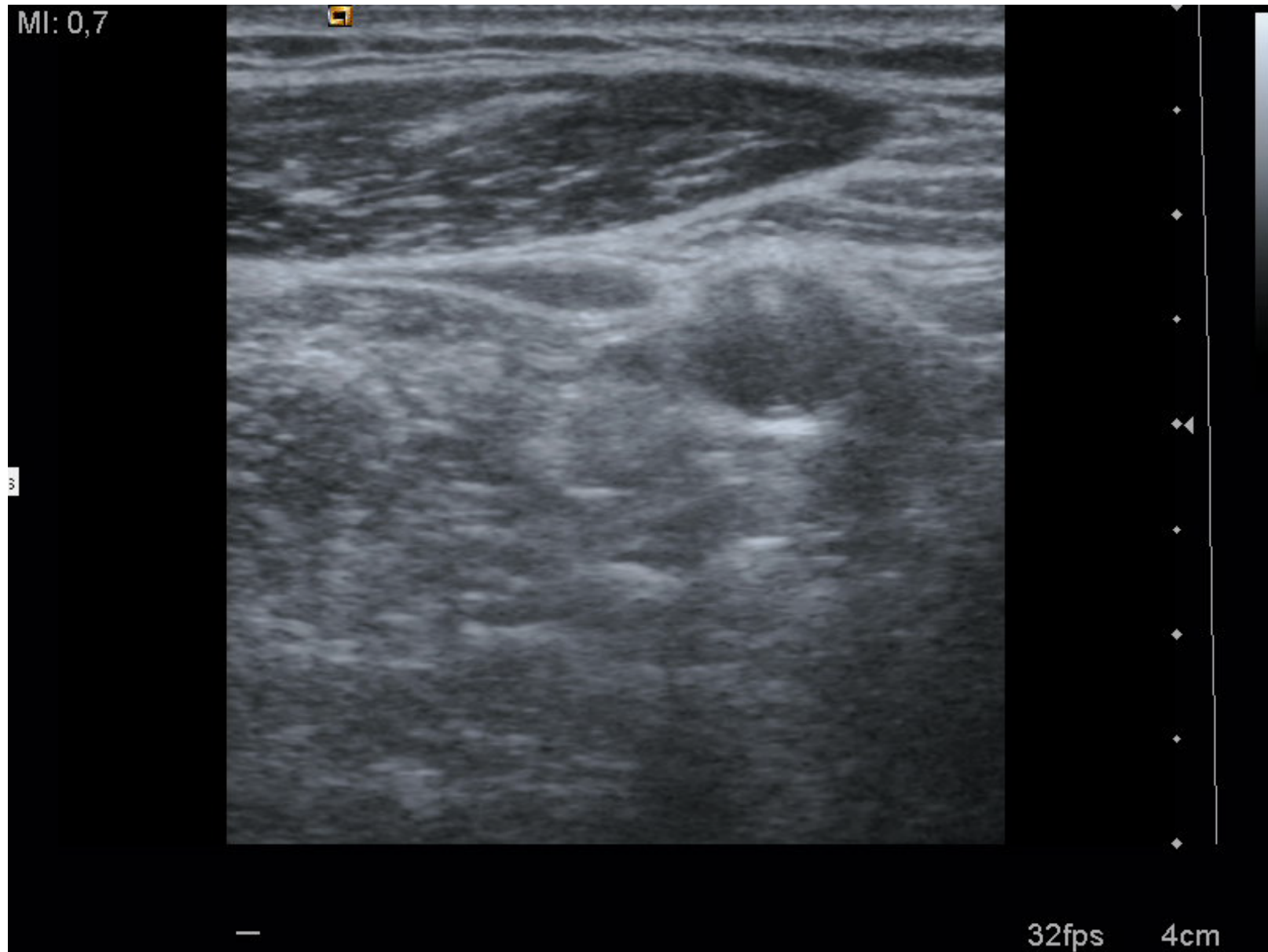
TIS: 1,3
TIB: 1,3



6
6
cm/s

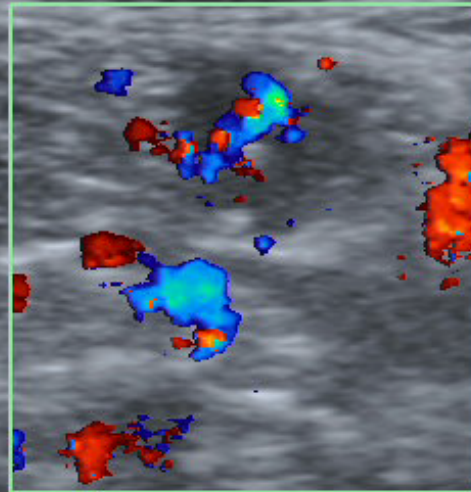
14fps 4cm

(SS)



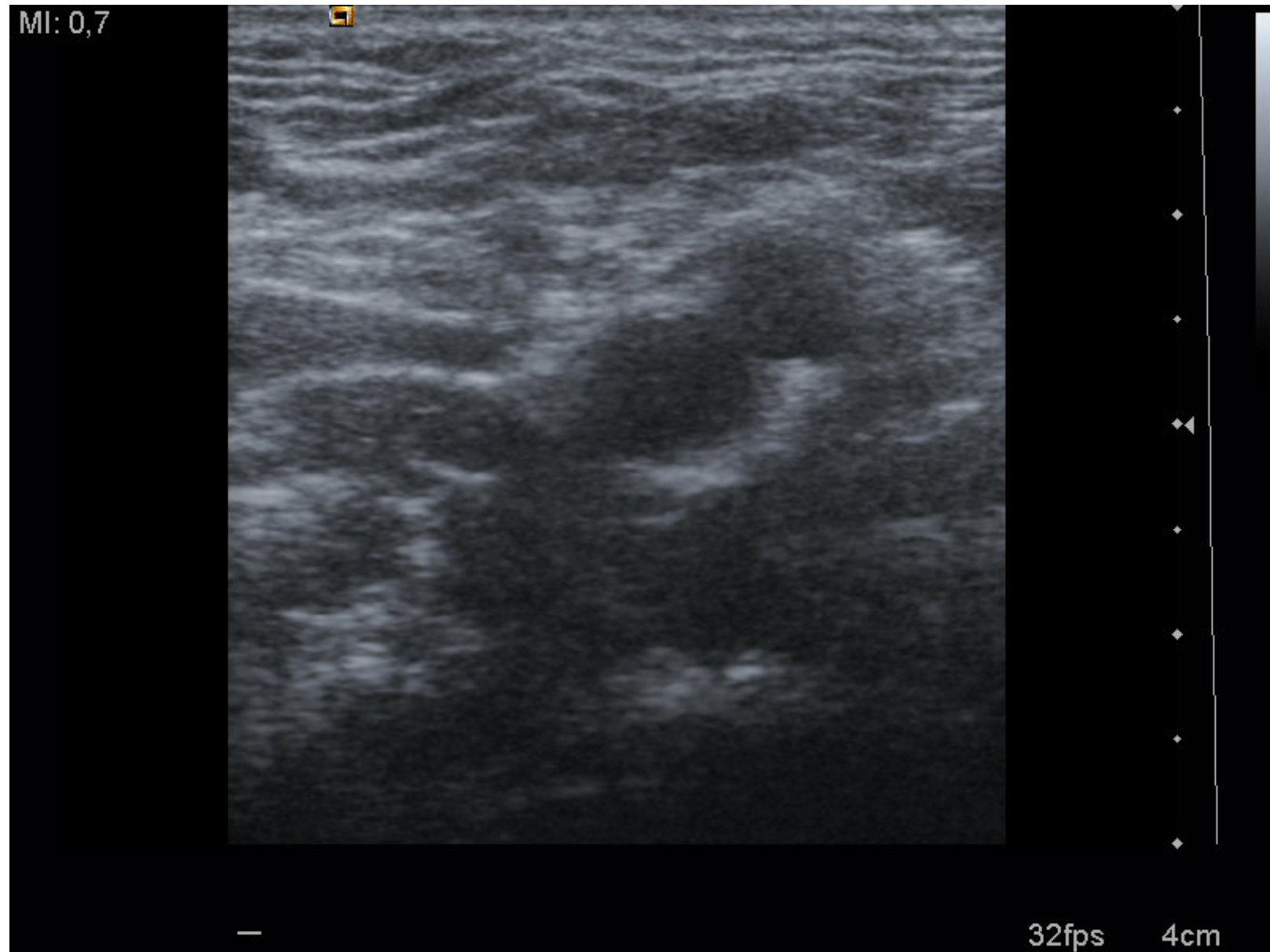
(SS)

TIS: 1,3
TIB: 1,3



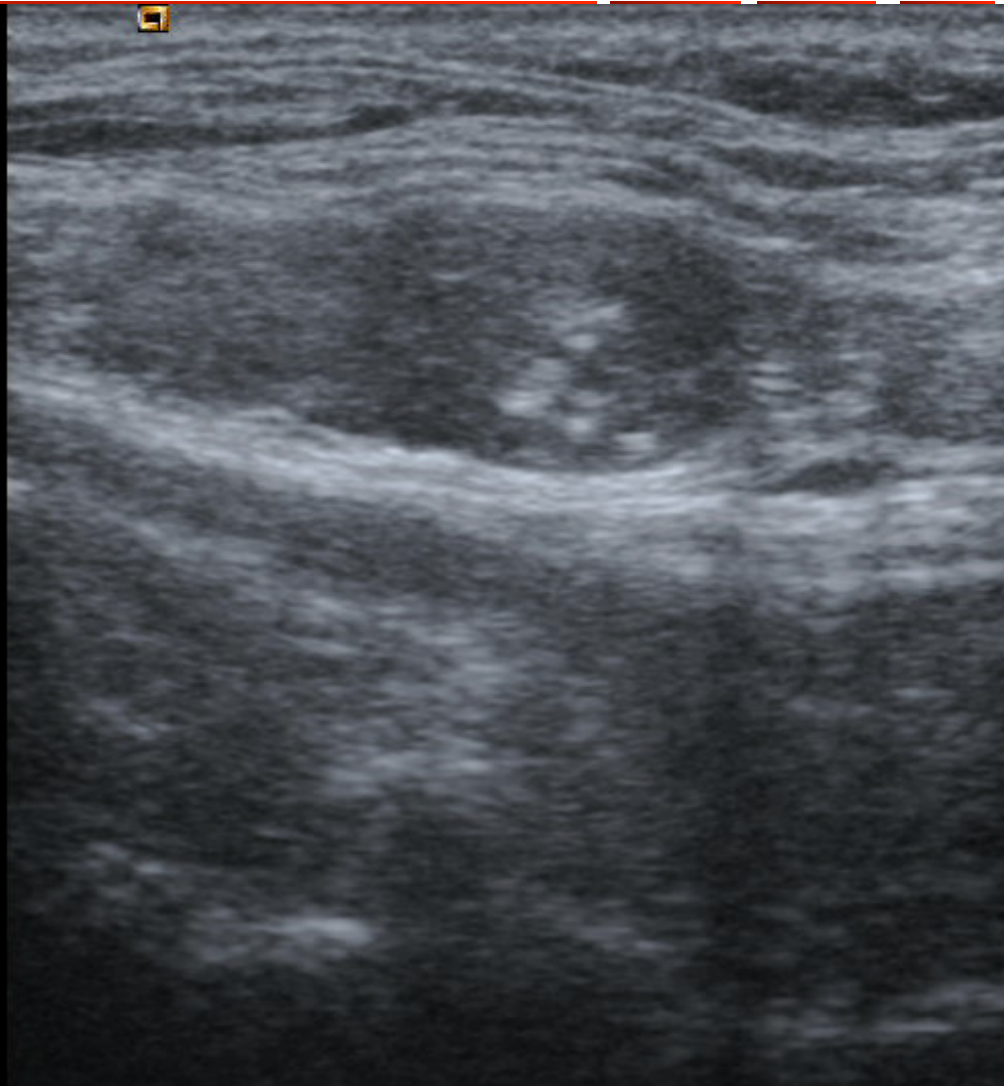
14fps 4cm

(SS)



(SS)

MI: 0,7



32fps

4cm

(SS)

- Sağ lobda papiller karsinom klasik tip
- Tümör çapı 12 mm, LVI var
- Tümör dışı dokuda kronik tiroidit
- 4/20 sağ lateral servikal metastaz, 25 mm, tümü metastatik
- 3/7 santral metastatik lenf nodu, 7 mm, tümü metastatik

(SS)

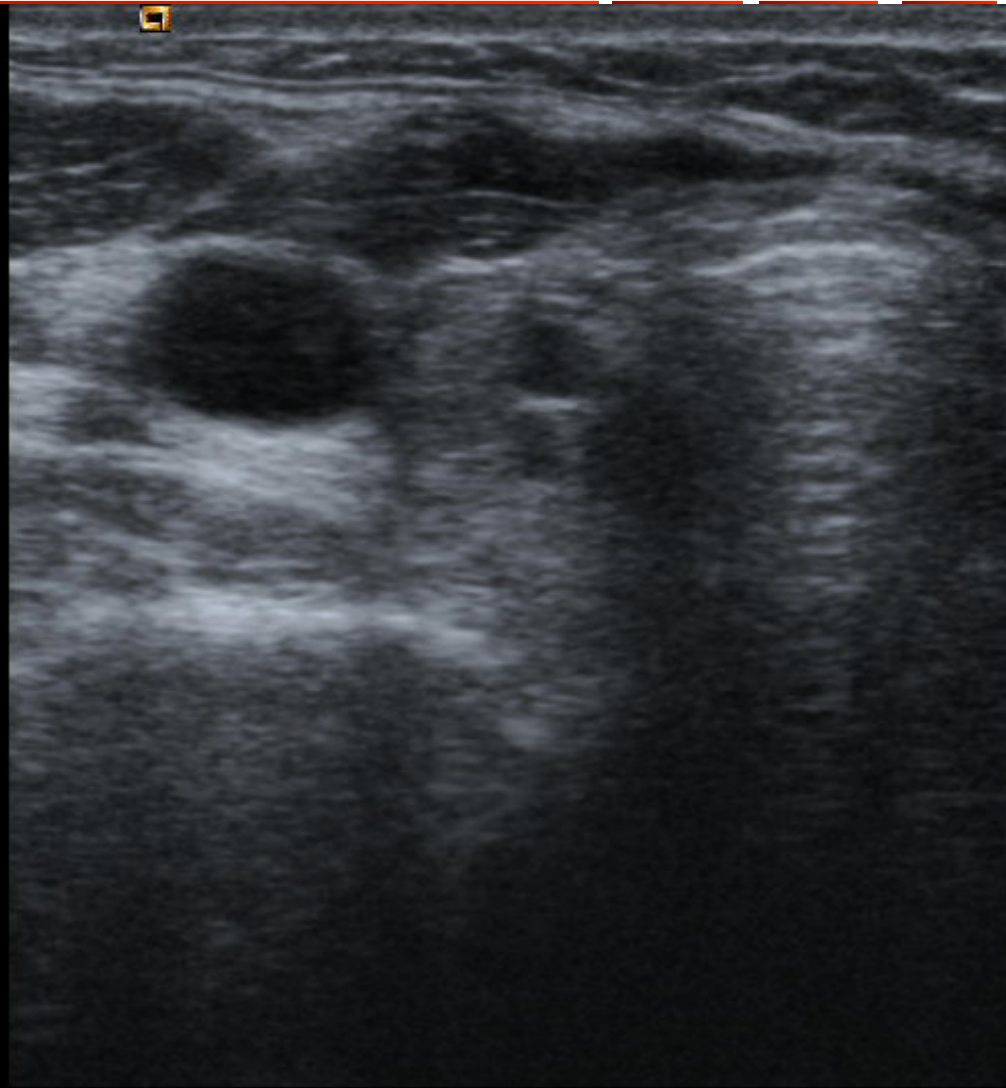
- Postop 6. hafta boyun US normal
- TSH 66.68 μ IU/mL
- Tg 0.156 ng/mL
- Tg-Ab negatif
- Düşük doz ablasyon – Ablasyonsuz takip önerildi
- Hasta tercihi ile ablasyonsuz takip

(FU)

- 40 yaşında kadın
- Sağ servikal lenf nodu İİAB malignite şüphesi

(FU)

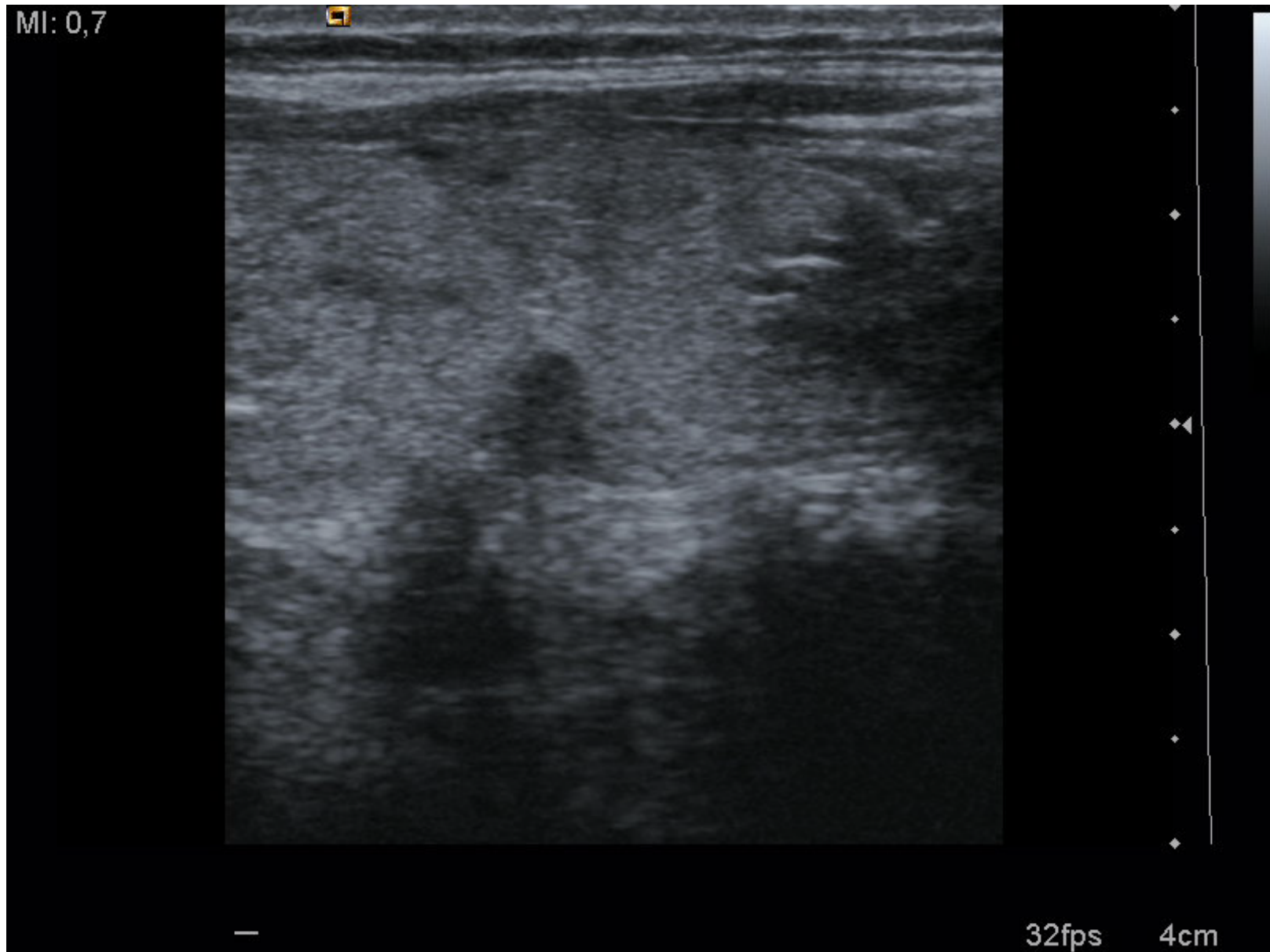
MI: 0,7



32fps

4cm

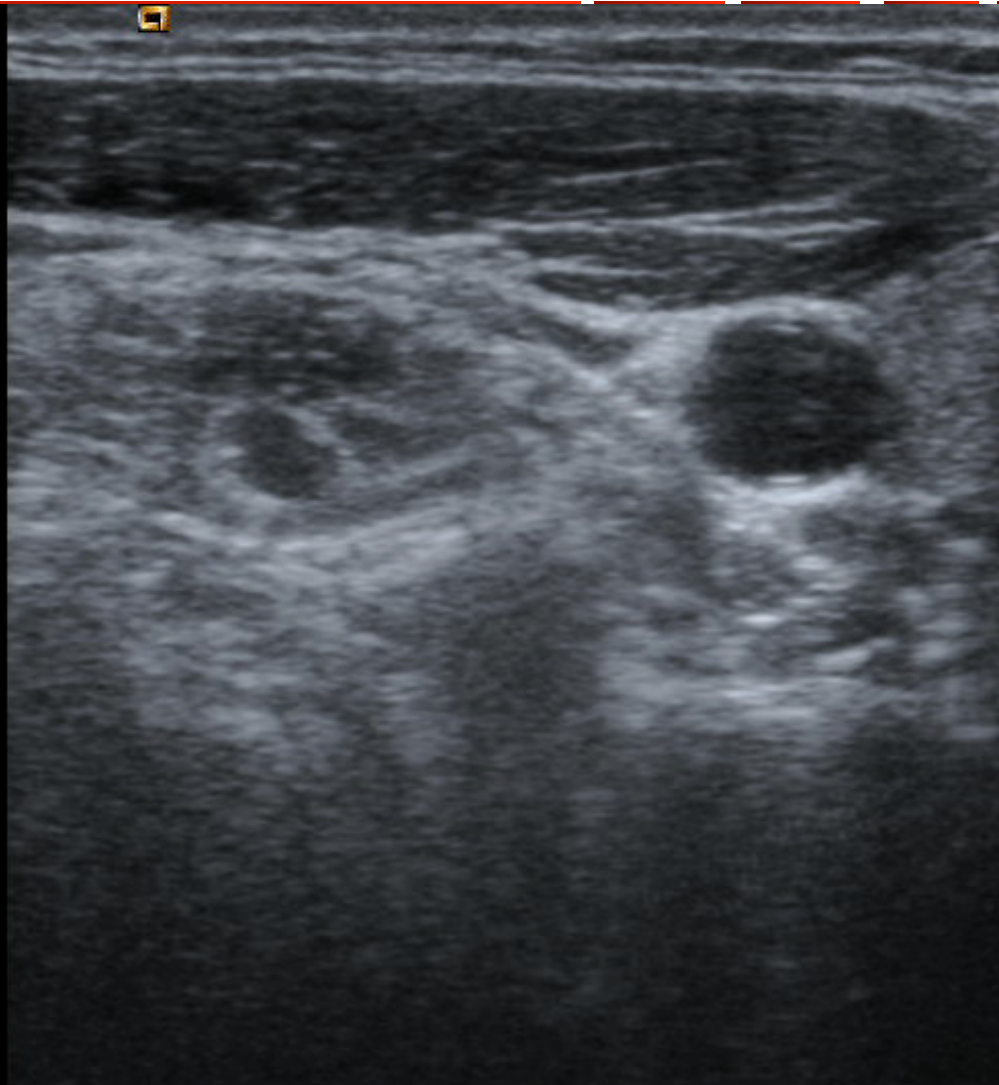
(FU)



(FU)

MI: 0,7

3

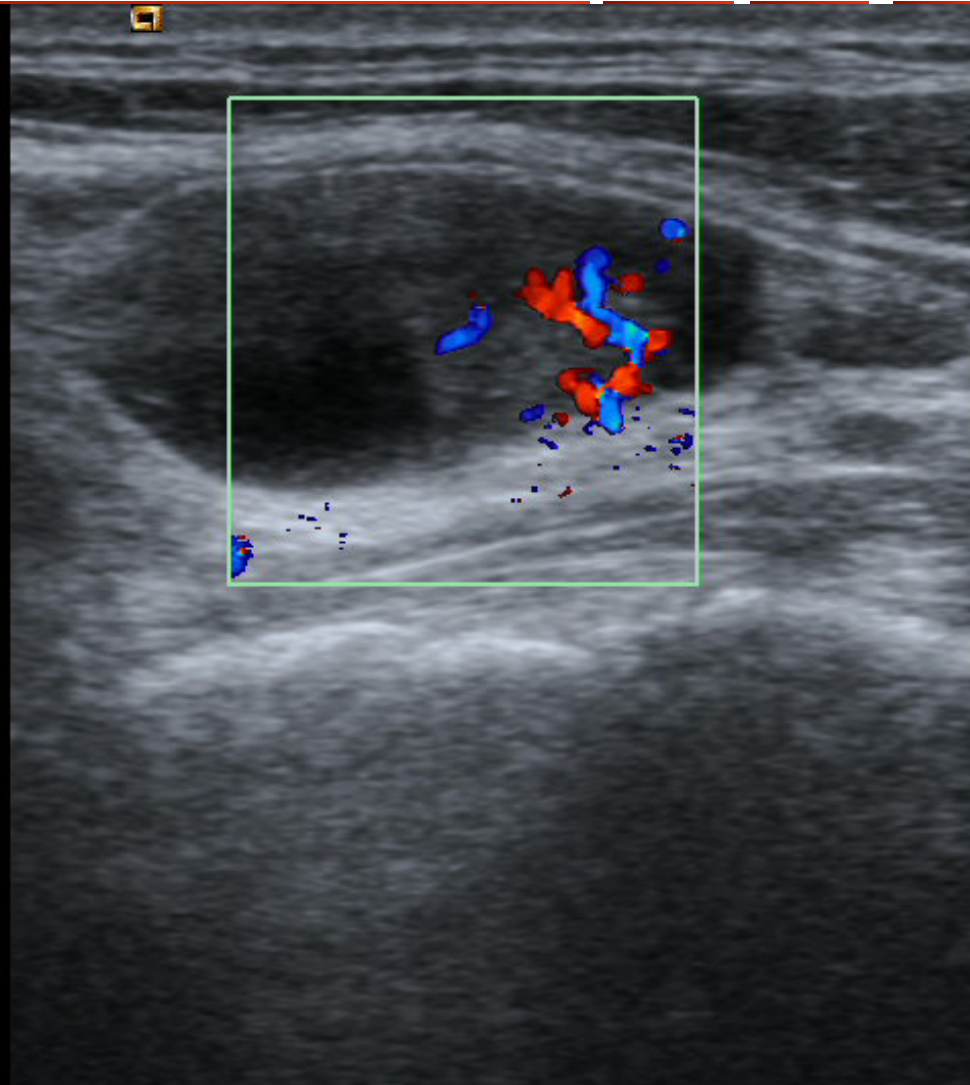


32fps

4cm

(FU)

TIS: 1,3
TIB: 1,3

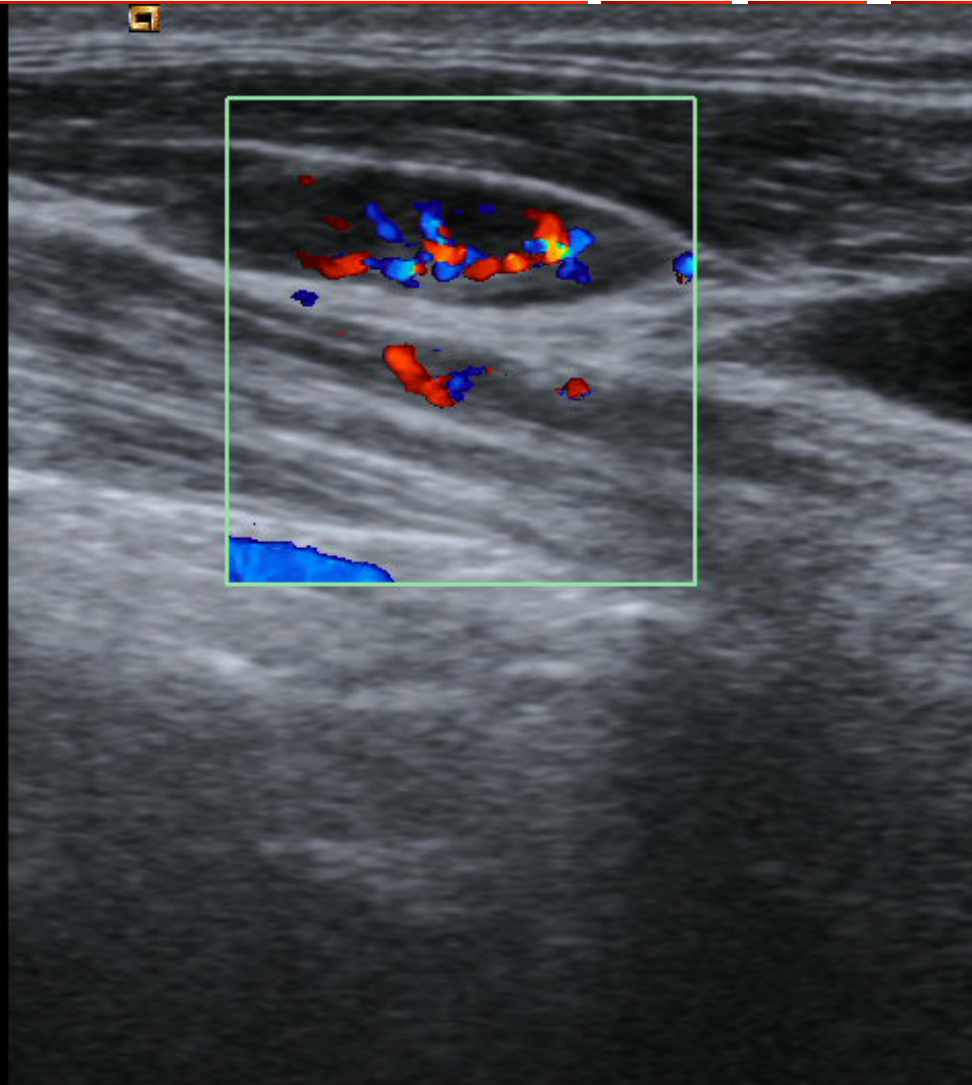


6
6
cm/s

14fps 4cm

(FU)

TIS: 1,3
TIB: 1,3



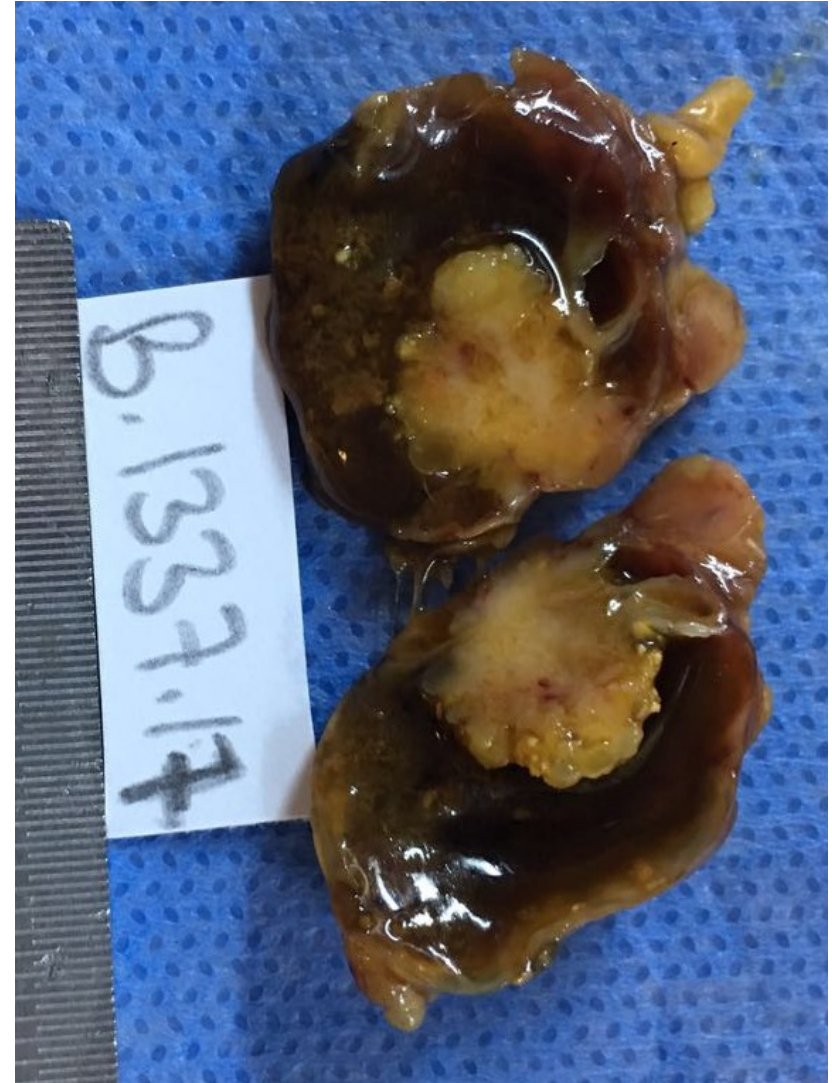
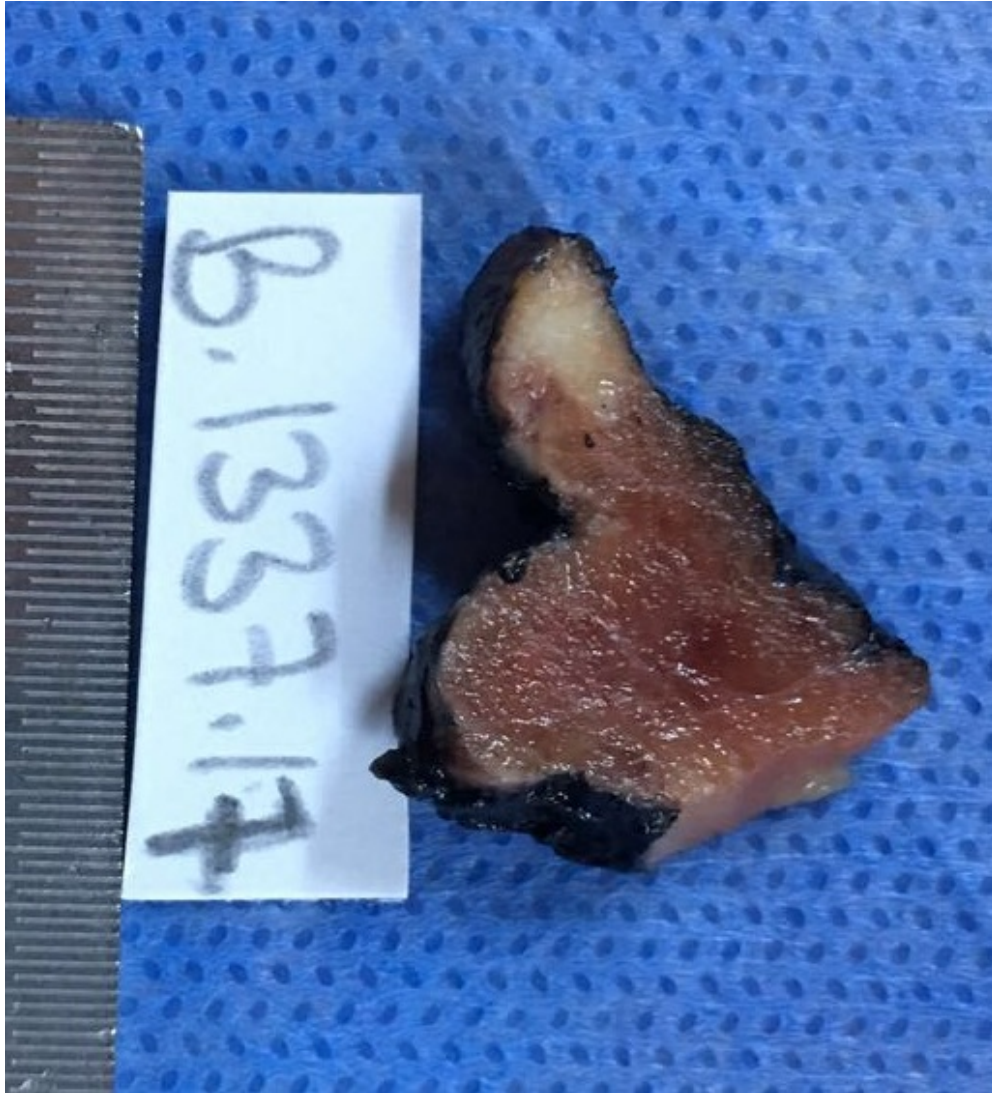
6
6
cm/s

14fps 4cm

(FU)

- 40 yaşında kadın
- Sağ lobda 8 mm papiller karsinom
 - Warthin benzeri tip
 - %50 hobnail komponent
 - Boyalı cerrahi sınırdan var, LVI pozitif
- İsthmusta 3 mm folliküler tip
- Tümör dışı dokuda kronik lenfositik tiroidit
- 1/18 sağ lateral metastaz
 - 25 mm tümü metastatik
- 19 reaktif santral lenf nodu

(FU)



(FU)

- Postop 6. hafta
- TSH > 100 μ IU/mL
- Tg 0.442 ng/mL
- Tg-Ab 163 IU/mL (Normali 0-115 IU/mL)
- 30 mCi I-131 ablasyonu
- I-131 tarama normal
- Tg < 0.1 ng/mL, Tg-Ab negatif, boyun US
- Postop 1. yıl

Düşük Risk Grubunda I-131 Kullanımı

ABLASYON

Düşük risk grubu / I-131 Ablasyon

■ RECOMMENDATION 51 (details in Table 14)

(A) RAI remnant ablation is not routinely recommended after thyroidectomy for ATA low-risk DTC patients. Consideration of specific features of the individual patient that could modulate recurrence risk, disease follow-up implications, and patient preferences are relevant to RAI decision-making.

(Weak recommendation, Low-quality evidence)

(B) RAI remnant ablation is not routinely recommended after lobectomy or total thyroidectomy for patients with unifocal papillary microcarcinoma, in the absence of other adverse features.

(Strong recommendation, Moderate-quality evidence)

(C) RAI remnant ablation is not routinely recommended after thyroidectomy for patients with multifocal papillary microcarcinoma in absence of other adverse features. Consideration of specific features of the individual patient that could modulate recurrence risk, disease follow-up implications, and patient preferences are relevant to RAI decision-making.

(Weak recommendation, Low-quality evidence)

Guidelines for radioiodine therapy of differentiated thyroid cancer

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-008-0883-1

Ablation

Due to the generally favourable prognosis of DTC, the impact of radioiodine ablation on disease-specific mortality and relapse rate is hard to substantiate. Few randomised studies address this topic, and some of these studies are inconclusive. However, a recent meta-analysis documented the positive influence of RAIT as an adjunct to thyroidectomy, namely, in retrospective studies with follow-up of 10 years or more [20]. When thyroid surgery is performed in highly expert hands at selected tertiary referral centres, though, the positive influence of radioiodine ablation may not be apparent [24].

Radioiodine ablation after total or near-total thyroidectomy is a standard procedure in patients with DTC. The only exception is patients with unifocal papillary thyroid carcinoma ≤ 1 cm in diameter who lack:

- evidence of metastasis,
- thyroid capsule invasion,
- history of radiation exposure,
- unfavourable histology:
 - tall-cell, columnar cell or diffuse sclerosing subtypes.

ATA -2015

TABLE 11. ATA 2009 RISK STRATIFICATION SYSTEM WITH PROPOSED MODIFICATIONS

ATA low risk	Papillary thyroid cancer (with all of the following): • No local or distant metastases; • All macroscopic tumor has been resected • No tumor invasion of loco-regional tissues or structures • The tumor does not have aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma) • If ^{131}I is given, there are no RAI-avid metastatic foci outside the thyroid bed on the first posttreatment whole-body RAI scan • No vascular invasion • Clinical N0 or ≤ 5 pathologic N1 micrometastases (< 0.2 cm in largest dimension)^a Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer^a Intrathyroidal, well differentiated follicular thyroid cancer with capsular invasion and no or minimal (< 4 foci) vascular invasion^a Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including <i>BRAF</i>^{V600E} mutated (if known)^a
ATA intermediate risk	Microscopic invasion of tumor into the perithyroidal soft tissues RAI-avid metastatic foci in the neck on the first posttreatment whole-body RAI scan Aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma) Papillary thyroid cancer with vascular invasion Clinical N1 or > 5 pathologic N1 with all involved lymph nodes < 3 cm in largest dimension^a Multifocal papillary microcarcinoma with ETE and <i>BRAF</i>^{V600E} mutated (if known)^a
ATA high risk	Macroscopic invasion of tumor into the perithyroidal soft tissues (gross ETE) Incomplete tumor resection Distant metastases Postoperative serum thyroglobulin suggestive of distant metastases Pathologic N1 with any metastatic lymph node ≥ 3 cm in largest dimension^a Follicular thyroid cancer with extensive vascular invasion (> 4 foci of vascular invasion)^a

ATA – Düşük Risk Grubu

- Papiller karsinom
 - Bölgesel/uzak metastaz yok
 - Tüm makroskopik tümör çıkartılmış
 - Ekstratiroidal yayılım yok
 - Agresif histopatoloji yok
 - I-131 verilmişse tiroid yatağı dışında iyot tutan metastatik odak yok
 - Vasküler invazyon yok
 - Klinik N0 veya ≤ 5 patolojik N1 mikrometastaz (0.2 cm en geniş çap)
- İntratiroidal enkapsüle folliküler varyant papiller karsinom
- İntratiroidal folliküler karsinom kapsüler invazyon mevcut, vasküler invazyon yok veya minimal
- İntratiroidal unifokal/multifokal papiller mikrokarsinom (BRAF mutasyonu dahil)

Düşük risk grubu

- Hızlı artışın önemli bir kısmı düşük risk grubu
- Madem düşük riskli neden takip ediyoruz ?
- Niye ablasyon yapalım ?

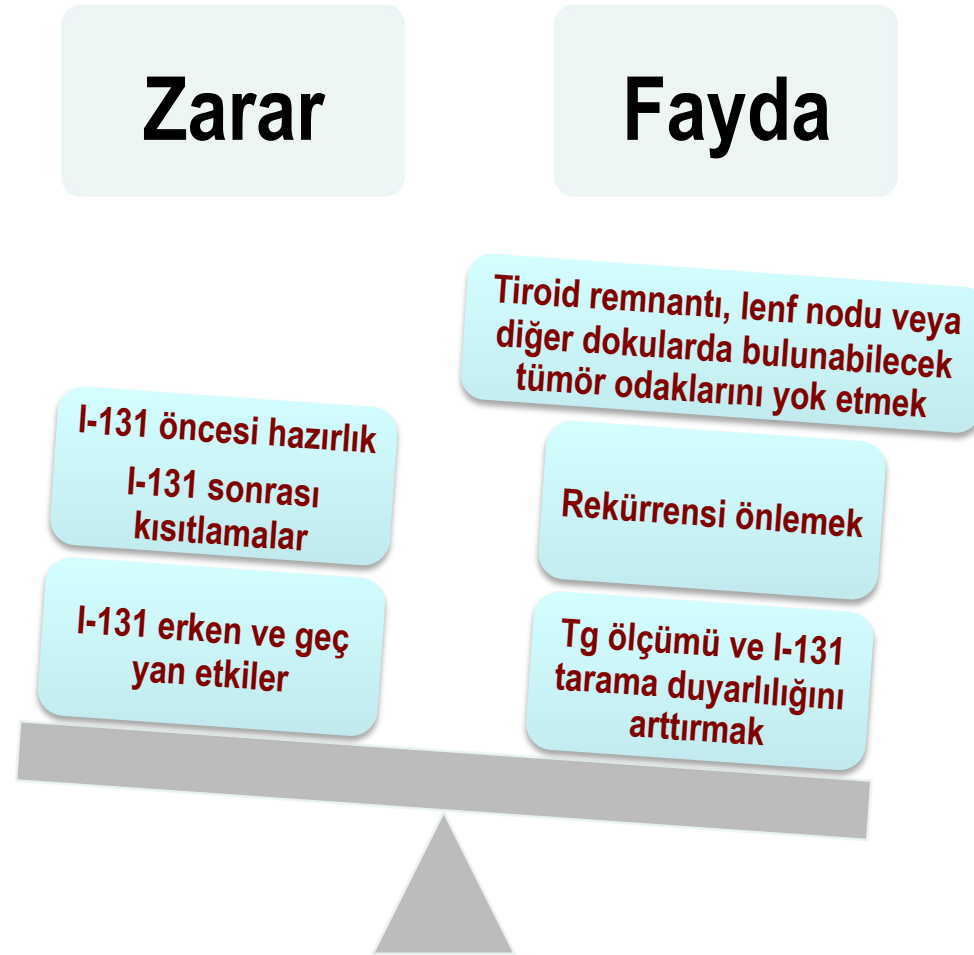
Ablatif amaçlı I-131 Kullanımı

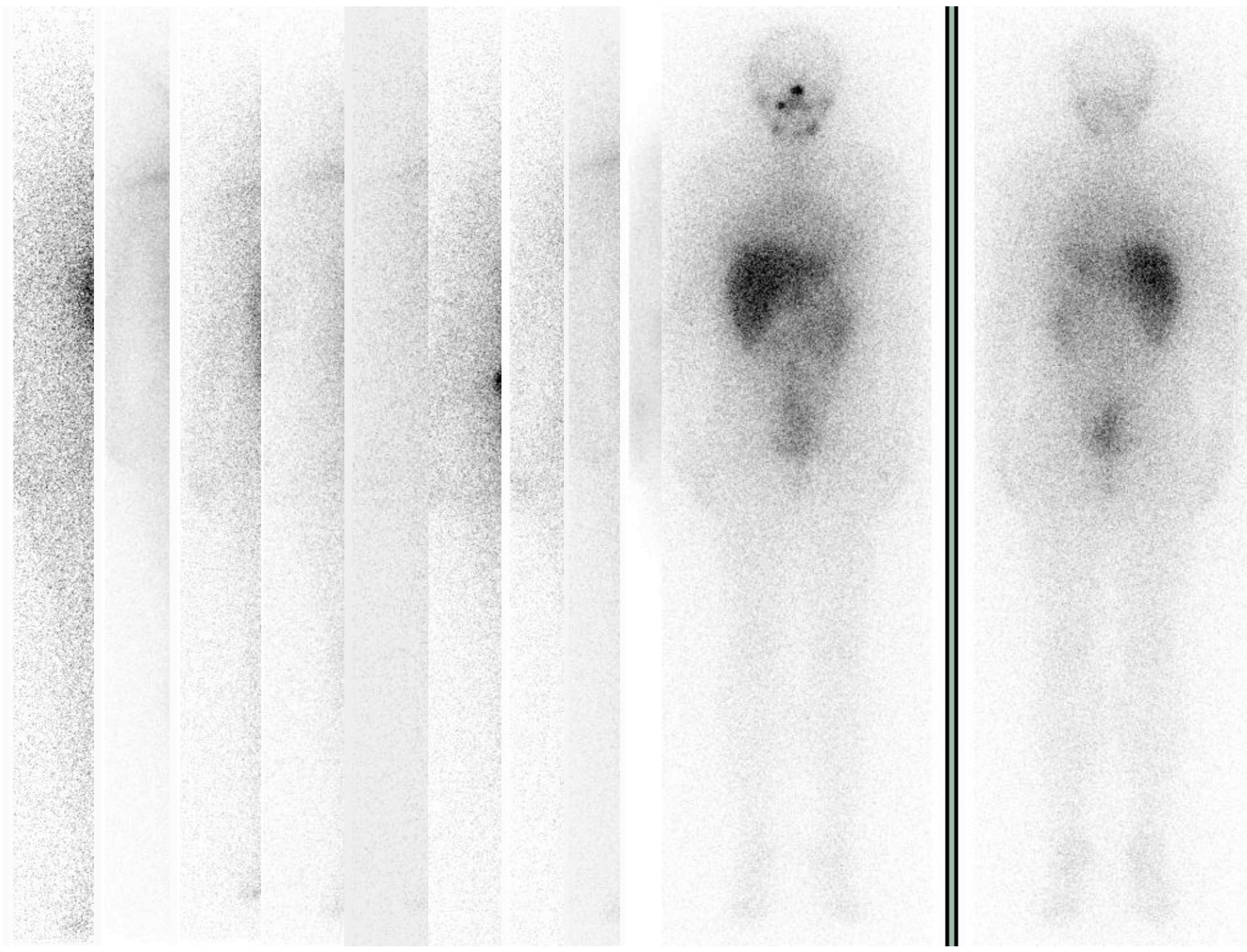
- Ablasyon konusunda karar verebilmek için
 - Takip stratejisi
 - Remnant ablasyonunun yan etkileri

Remnant ablasyonu

- Gerekli değildir !
 - Düşük risk grubunda yaşam süresini etkilediği gösterilmemiştir
- Gereklidir !
 - Ablasyon yapılmadan Tg duyarlı bir tümör belirteçi olmaz
 - Rezidüel doku I-131 Tarama duyarlılığını azaltır
 - *Normal dokunun I-131 uptake'i daha fazladır*
 - *Star artefakt / TSH yükselmeyeblir*
 - Rezidüel dokudaki olası malign hücreler yok edilir
 - Rezidüel dokuda malign transformasyon olasılığı ortadan kalkar
 - Remnant ablasyonu bölgesel nüks ve metastaz olasılığını azaltır

Düşük Risk Grubunda Ablasyon Kararı





Düşük risk grubu

- Ablasyon takibi kolaylaştırır mı?

Tiroid Kanserinde Takip

- Risk gruplarının izlem üzerine etkisi daha az belirgin
- Tüm hasta gruplarında ömür boyu izlem
- Takip aralıkları en uzun 12-24 ay
- Takipte fizik muayenenin yeri ?

Tg ölçümü

- Cerrahi ve RAI ablasyonu sonrası
 - Mükemmel tümör belirteci (medüller ve anaplastik dışında)
- Görece objektif
- Tercihen aynı laboratuvar- aynı yöntem
- Yalancı negatif sonuçlar
 - Tg antikorları pozitifliği
 - Aşırı yüksek Tg (hook effect)
- Tg – TSH ilişkisi
 - Supresyon altında 0.2-0.3 ng/mL
 - Stimüle Tg < 1 ng/mL, < 2 ng/mL, < 10 ng/mL

Tg ölçümü

- Lobektomili olgularda eşik değer ?
- I-131 ablasyonu yapılmayan olgularda eşik değer ?
- Tg antikoru pozitif düşük risk grubunun yönetimi ?

Boyun US

- Lobektomili veya ablasyon yapılmayan olgularda temel izlem yöntemi
- Sonografi
 - Subjektif
 - Tüm klinik ve biyokimyasal verilerle birlikte değerlendirilmeli
 - Nodal metastaz için güvenilir kriterler az ve geç dönemde oluşur
 - Mikrokalsifikasyon, kistik dejenerasyon, eko artışı, patolojik kanlanma
 - Santral lenf nodlarının değerlendirilmesi daha zor
- Şüpheli lenf nodlarından yapılan aspiratların yarısı normal
 - Zayıf kriterler sık izlenir
 - Boyut, sinüs ekosunun silinmesi, kortikal kalınlaşma

Boyun US

- Düşük risk grubunda ablasyonsuz izlemde
- Tg 0.7 ng/mL, Tg-Ab negatif
- İpsilateral segment III 14x6 mm ve 16x7 mm boyutlarında sinüsü silik, kalın korteksli lenf nodları

- Düşük risk grubunda ablasyon yapılmış
- Tg < 0.1 ng/mL, Tg-Ab negatif
- İpsilateral segment III 14x6 mm ve 16x7 mm boyutlarında sinüsü silik, kalın korteksli lenf nodları

- Düşük risk grubunda ablasyon yapılmış
- Tg 0.7 ng/mL, Tg-Ab negatif
- İpsilateral segment III 14x6 mm ve 16x7 mm boyutlarında sinüsü silik, kalın korteksli lenf nodları

I-131 Tüm Vücut Tarama

- Tanısal / tedavi sonrası
- Spesifik tutulum mekanizması
- Tedavi sonrası taramalar
 - Servikal/estraservikal metastaz – başlangıç evrelemesi
 - Stimüle Tg negatifken bile metastaz saptanabilir
- Tanısal taramaların etkinliği düşük
 - US + Tg ölçümüne katkısı sınırlı
- Ablasyon yapılmayan olgularda katkısı yok

Diğer Görüntüleme Yöntemleri

- FDG PET
- I-124 PET
- BT
- MRG

I-131 - Yan Etki / Komplikasyon



L-T4 Supresyon tedavisinin potansiyel istenmeyen etkileri

- Kemik mineral yoğunluğunda azalma
- Kardiyovasküler etkiler
 - Atrial fibrilasyon riskinde artış
 - Kalp hızında artış
 - Atrial prematür kontraksiyon
 - Kardiyak kontraktilite artışı
 - Ventriküler hipertrofi
 - Sistolik/diastolik disfonksiyon
 - Kardiyovasküler mortalite artışı

Cerrahiye baėlı komplikasyonlar

- Kanama ve hematom
- Yara enfeksiyonu
- Ses kısıklığı
- Hipokalsemi
- Cilt yanığı
- Ösefagus ve trakea perforasyonu
- Cerrahi ve anesteziye baėlı diėer riskler

I-131 - Yan Etki / Komplikasyon

- Bulantı / kusma
 - En sık yan etki (%50)
 - En sık 7-12 saat sonra başlar – 24-36 saat sonra düzelir
 - Parietal hücrelerde I-131 akümülyasyonuna bağlı radyasyon gastriti
 - Dozla olasılığı artar (> 100 mCi)
- Tad duyu bozukluğu
 - Majör ve minör tükürük bezlerinde iyot akümülyasyonu
 - Bir gün sonra başlayan ve 1 hafta kadar süren tad duyusu bozukluğu
 - Von Ebner bezlerinde radyasyon hasarı / majör tükürük bezlerinde sekresyon ve kompozisyon değişikliği

I-131 - Yan Etki / Komplikasyon

- Tükürük bezlerinde şişme
 - Yüksek doz alanların yaklaşık %30'unda şişlik ve hassasiyet
 - Seröz bezlerin parankimal hücrelerinde radyasyon hasarı
 - Bir hafta içinde kendiliğinden düzelir
 - Hidrasyon, analjezik ve tükürük stimülasyonu, gerekirse steroid
 - Takip eden yıl içinde ağrısız şişlik, kanal darlığı ve tuzlu akıntı
- Tiroid lojunda ödem
- Akut radyasyon hastalığı
 - Baş ağrısı, kırgınlık, bulantı (> 200 mCi)

I-131 - Yan Etki / Komplikasyon

- Ağız kuruluğu ve dental problemler
 - Yüksek doz alanların (500 mCi) yaklaşık %80'inde
 - 375 mCi I-131 uygulananların %75'inde tükürük salgısında %40 azalma
 - Tükürük salgısı azalanların büyük kısmı asemptomatik
 - Diş problemleri daha sık
- Nazolakrimal kanal obstrüksiyonu
- Konjoktivit ve göz kuruluğu
- Epistaksis

I-131 - Yan Etki / Komplikasyon

- Menstrüel siklus düzensizliği ve erken menapoz
 - Yaş ve uygulanan aktivite önemli
- Kadınlarda infertilite, düşük, prematürite ve doğumsal defekt
 - Standart dozlarda(< 200 mCi) fertilite, doğum ağırlığı ve doğumsal defektle ilişkisi yok
- Testiküler hasar, infertilite ve doğumsal defekt
 - Geçici FSH yüksekliği ve sperm kalitesinde bozulma
 - Uzamış ve kalıcı oligospermi yüksek kümülatif dozlarda (> 500 mCi)
 - 500-1000 mCi dozlarda bile çoğunlukla fertilite korunur

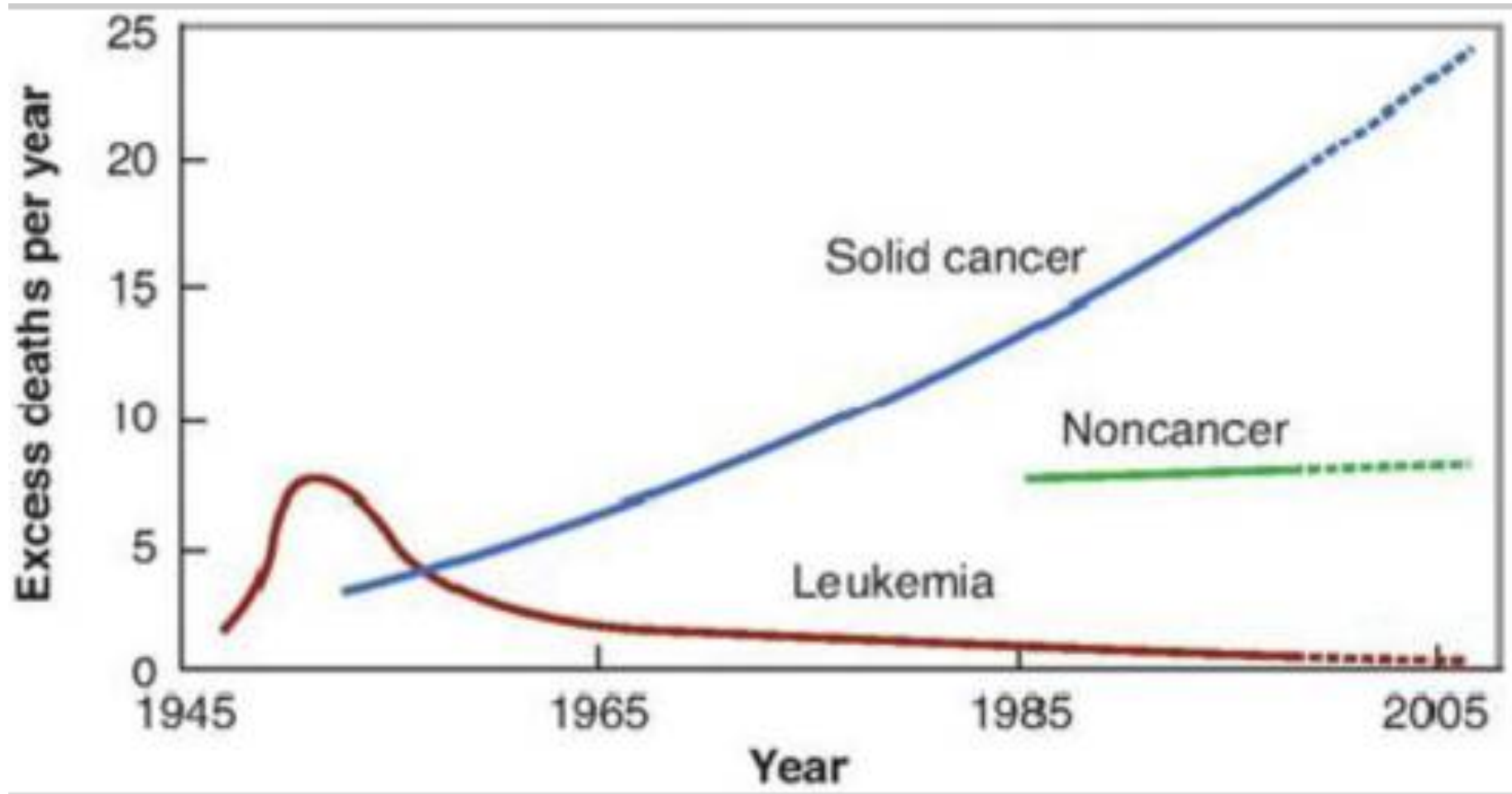
I-131 - Yan Etki / Komplikasyon

- Tiroidit / Tirotoksikoz
 - Fazla remnant
- Geçici kemik iliği supresyonu
 - 4-6 haftada en düşük, 12 haftada düzelir
- Klinik olarak önemli kemik iliği supresyonu
 - Böbrek yetmezliği, ileri yaş, sık I-131 uygulaması
- Stomatit

I-131 - Yan Etki / Komplikasyon

- İkincil maligniteler
 - Bir kısım hastada lösemi ve solid tümör gelişimi (tükrük bezi)
 - Doz arttıkça risk artar (kümülatif doz > 500-1.000 mCi)
 - Birçok çalışmada kontrol grubu normal popülasyon

Atom Bombası Kazazedeleri



I-131 - Yan Etki / Komplikasyon

- Yan etki profili eksternal radyoterapi ve sitotoksik kemoterapiden daha üstün
- Her bir klinik durum için fayda/zarar oranı çerçevesinde değerlendirilmeli
- Doğru gerekçelendirme

I-131 - Yan Etki / Komplikasyon

- Yan etkilerin önemli bir kısmı tekrarlanan ve kümülatif olarak yüksek dozlarda
- Doz arttıkça görülme sıklıkları artar
- Yüksek risk grubunda yan etkiler potansiyel fayda yanında önemsiz
- Ablatif dozlarda yan etki az
- Ablatif doz yan etkileri ile ilgili çalışma az

Ablasyon 30 vs 100 mCi

- Başarılı ablasyon oranları düşük dozda %5 daha az
- 100 mCi ablasyonda daha başarılıdır
 - Avrupa sonuçları
 - Total tiroidektomiden daha az cerrahiler
- Genel olarak 30 mCi 100 mCi kadar başarılı

Ablasyonda düşük/yüksek doz

Nucl Med Commun. 2012 Mar;33(3):275-82. doi: 10.1097/MNM.0b013e32834e306a.

Low versus high radioiodine dose in postoperative ablation of residual thyroid tissue in patients with differentiated thyroid carcinoma: a large randomized clinical trial.

Fallahi B¹, Beiki D, Takavar A, Fard-Esfahani A, Gilani KA, Saghari M, Eftekhari M.

⊕ Author information

Abstract

OBJECTIVES: Radioiodine ablation of thyroid tissue remains the cornerstone of treatment for patients with differentiated thyroid carcinoma after thyroidectomy. Selecting an optimal dose of radioiodine for successful ablation is a continuous challenge in these patients.

METHODS: We compared the treatment response of 341 patients with thyroidectomy randomly allocated to the high-dose group, 3700 MBq (170 patients), versus the low-dose group, 1110 MBq (171 patients), for radioiodine ablation therapy in a double-blind randomized clinical trial. The response to treatment was defined as successful or unsuccessful according to post-therapy ultrasonography of the neck, serum thyroglobulin (Tg), anti-Tg, and functioning residual tissue after 6-month and 12-month intervals. The major criteria of successful ablation were Tg<2 ng/ml, anti-Tg<100 IU/ml, and absent remnant in the off-levothyroxine state. Additional radioiodine doses were administered in cases showing no significant response to the first therapy. Finally, the initial outcome, the total hospitalization time, and the cumulative I-131 doses during the 12-month course of the study were compared between the subgroups.

RESULTS: The rate of initial successful ablation was 51.6% in all patients, 39.2% in the low-dose group, and 64.1% in the high-dose group. The corresponding success rates at the end of the 12-month follow-up without additional treatment were 55.1, 41.5, and 68.8%, respectively. The relative risk (RR) of unsuccessful ablation for the low-dose versus the high-dose group was 1.695 [95% confidence interval (CI), 1.34-2.14]. In the low-dose group, more patients needed a second dose of I-131, resulting in a higher cumulative activity (median, 4810 vs. 3700 MBq, P<0.0001) and more inpatient time (median 4 vs. 3 days) in comparison with the high-dose group. The covariate factors predicting the treatment response, in order of significance, were radioiodine dose, baseline Tg, baseline thyroid stimulating hormone (TSH) level, efficiency of TSH suppressive therapy, and sex.

CONCLUSION: The higher dose of I-131 (3700 MBq) resulted in successful ablation more often than the low dose (1110 MBq).

Ablasyonda düşük/yüksek doz

PLoS One. 2008 Apr 2;3(4):e1885. doi: 10.1371/journal.pone.0001885.

Low vs. high radioiodine activity to ablate the thyroid after thyroidectomy for cancer: a randomized study.

Mäenpää HO¹, Heikkinen J, Vaalavirta L, Tenhunen M, Joensuu H.

⊕ Author information

Abstract

BACKGROUND: Radioactive iodine is commonly administered following thyroidectomy for differentiated thyroid carcinoma to ablate the thyroid remnant. The optimal administered activity of radioiodine is unknown.

METHODOLOGY/PRINCIPAL FINDINGS: Adult subjects (n = 160) diagnosed with papillary or follicular thyroid carcinoma were randomly allocated to receive either 1100 MBq (30 mCi) or 3700 MBq (100 mCi) activity of radioiodine (¹³¹I) following thyroidectomy. The study participants were prepared for ablation using thyroid hormone withdrawal. Ablation was considered successful when serum thyroglobulin concentration was less than 1 ng/mL and no uptake was present in ¹³¹I scan. Ablation was successful following one administration of radioiodine in 42 (52%; 95% CI, 41% to 63%) of the 81 evaluable study participants who received 1100 MBq, and in 43 (56%, 45% to 67%) of the 77 subjects who received 3700 MBq activity (P = .61). There was no difference between the groups in the numbers of repeat radioiodine treatments needed to complete ablation (P = .27). The higher activity was associated with more nausea and taste disturbances, and a longer stay in a radioprotected isolation unit. None of the participants died from thyroid cancer during a median follow up of 51 months; three subjects in the 3700 MBq group and none in the 1100 MBq group were diagnosed with distant metastases during follow-up. In a meta-analysis of four randomized studies that compared the 1100 and 3700 MBq activities, the 1100 MBq activity tended to be associated with a higher risk of unsuccessful ablation (relative risk 1.148, 95% CI 0.974 to 1.353, P = .10).

CONCLUSIONS/SIGNIFICANCE: The results provide no conclusive evidence that 3700 MBq activity is more effective for ablation of the thyroid remnant than 1100 MBq activity. The 3700 MBq activity is associated with more adverse effects.

TRIAL REGISTRATION: ClinicalTrials.gov [NCT00115895](https://clinicaltrials.gov/ct2/show/study/NCT00115895).

Ablasyonda düşük/yüksek doz

J Clin Endocrinol Metab. 2013 Apr;98(4):1353-60. doi: 10.1210/jc.2012-3682. Epub 2013 Feb 22.

Low- or high-dose radioiodine remnant ablation for differentiated thyroid carcinoma: a meta-analysis.

Cheng W¹, Ma C, Fu H, Li J, Chen S, Wu S, Wang H.

⊕ Author information

Abstract

CONTEXT: There is uncertainty over the dose of (131)I required for thyroid remnant ablation. Most previous studies have been inadequately powered to establish the best fixed dose of (131)I for effective ablation.

OBJECTIVE: The aim of the study was to assess the effects of low- vs high-dose regimens of radioiodine in thyroid remnant ablation for patients with differentiated thyroid carcinoma.

DATA SOURCES: Sources included the Cochrane Library, MEDLINE, EMBASE, and SCOPUS (all until September 2012).

STUDY SELECTION: Randomized controlled trials that assess the efficacy of low- or high-dose of radioiodine ablation of thyroid remnants were collected.

DATA EXTRACTION: Two authors performed the data extraction independently.

DATA SYNTHESIS: Nine randomized controlled trials involving 2569 patients were included. The 1100-MBq vs the 3700-MBq radioiodine showed no statistically significant difference in successful thyroid remnant ablation (risk ratio [RR], 0.91 [0.79 to 1.04]; $P = .15$), both the 1100 vs the 1850 MBq (RR, 0.95 [0.83 to 1.10]; $P = .52$) and the 1850 vs the 3700 MBq (RR, 1.00 [0.85 to 1.17]; $P = .98$) also showed no significant differences (95% confidence intervals were calculated for each estimate). Also, no significant differences existed in quality-of-life scores on the SF-36 between different (131)I-dose groups both on the day of ablation (RR, 0.15 [-0.65 to 0.96], $P = .71$; $I(2) = 29\%$, $P = .24$) and 3 months after ablation (RR, -1.1 [-2.37 to 0.17], $P = .09$; $I(2) = 22\%$, $P = .26$). A low dose of 1100 MBq radioiodine showed significant benefits in reducing adverse effects (total RR, 0.65 [0.55 to 0.77], $P < .1$; $I(2) = 31\%$, $P = .14$) and shorter hospital isolation (RR, 0.4 [0.32 to 0.50]; $P < .05$).

CONCLUSIONS: The low dose of 1100 MBq radioiodine activity is sufficient for thyroid remnant ablation as compared to 3700 MBq radioiodine activity with similar quality of life, less common adverse effects, and a shorter hospital stay.

ESTIMABL2

Differentiated Thyroid Cancer: is There a Need for Radioiodine Ablation in Low Risk Patients? (ESTIMABL2)

This study is currently recruiting participants. (see [Contacts and Locations](#))

Verified June 2016 by Gustave Roussy, Cancer Campus, Grand Paris

Sponsor:

Gustave Roussy, Cancer Campus, Grand Paris

Information provided by (Responsible Party):

Gustave Roussy, Cancer Campus, Grand Paris

ClinicalTrials.gov Identifier:

NCT01837745

First received: April 16, 2013

Last updated: June 8, 2016

Last verified: June 2016

[History of Changes](#)

[Full Text View](#)

[Tabular View](#)

[No Study Results Posted](#)

[Disclaimer](#)

[? How to Read a Study Record](#)

► Purpose

Open-label randomized phase III trial, using a non-inferiority comparison design. After randomization, patients will receive either post-operative radioiodine ablation with an activity of 1.1 GBq (30 mCi) after stimulation by rhTSH, and then be followed-up (ablation group) or be followed-up (without postoperative radioiodine ablation) (follow-up group).

The objective is to assess the non-inferiority of the proportion of patients without tumor-related event evaluated at three years after randomisation in the absence of radioiodine ablation (follow-up group) compared to the ablation group, in patients with low-risk differentiated thyroid cancer treated with total thyroidectomy with or without lymph node dissection (pT1a m N0 or Nx, pT1b N0 or Nx)

IoN

IoN- Is Ablative Radio-iodine Necessary for Low Risk Differentiated Thyroid Cancer Patients (IoN)

This study is currently recruiting participants. (see [Contacts and Locations](#))

Verified October 2016 by University College, London

Sponsor:

University College, London

Collaborator:

Cancer Research UK

Information provided by (Responsible Party):

University College, London

ClinicalTrials.gov Identifier:

NCT01398085

First received: July 6, 2011

Last updated: October 25, 2016

Last verified: October 2016

[History of Changes](#)

Full Text View

Tabular View

No Study Results Posted

[Disclaimer](#)

[? How to Read a Study Record](#)

► Purpose

IoN is a phase II/ III trial that will look to ascertain whether or not radio-iodine ablation is necessary for low risk differentiated thyroid cancer patients.

I-131 - Ablasyon kararı ne zaman verilmeli ?

- İyot uygulamak için ideal zamanlama nedir?
- İyot ablasyon kararı ertelenebilir mi?
- Erken uygulamazsak etkisi azalır mı?

Erken / Geç I-131 Uygulaması

Endocr Pract. 2016 Jul;22(7):822-31. doi: 10.4158/EP151088.OR. Epub 2016 Mar 28.

TIMING OF RADIOACTIVE IODINE THERAPY DOES NOT IMPACT OVERALL SURVIVAL IN HIGH-RISK PAPILLARY THYROID CARCINOMA.

Suman P, Wang CH, Abadin SS, Block R, Raghavan V, Moo-Young TA, Prinz RA, Winchester DJ.

Abstract

OBJECTIVE: Postthyroidectomy radioiodine (RAI) therapy is indicated for papillary thyroid carcinoma (PTC) with high-risk features. There is variability in the timing of RAI therapy with no consensus. We analyzed the impact of the timing of initial RAI therapy on overall survival (OS) in PTC.

METHODS: The National Cancer Data Base (NCDB) was queried from 2003 to 2006 for patients with PTC undergoing near/subtotal or total thyroidectomy and RAI therapy. High-risk patients had tumors >4 cm in size, lymph node involvement, or grossly positive margins. Early RAI was ≤3 months, whereas delayed was between 3 and 12 months after thyroidectomy. Kaplan-Meier (KM) and Cox survival analyses were performed after adjusting for patient and tumor-related variables. A propensity-matched set of high-risk patients after eliminating bias in RAI timing was also analyzed.

RESULTS: There were 9,706 patients in the high-risk group. The median survival was 74.7 months. KM analysis showed a survival benefit for early RAI in high-risk patients ($P = .025$). However, this difference disappeared (hazard ratio [HR] 1.26, 95% confidence interval [CI] 0.98-1.62, $P = .07$) on adjusted Cox multivariable analysis. Timing of RAI therapy failed to affect OS in propensity-matched high-risk patients (HR 1.09, 95% CI 0.75-1.58, $P = .662$).

CONCLUSION: The timing of postthyroidectomy initial RAI therapy does not affect OS in patients with high-risk PTC.

ABBREVIATIONS: CI = confidence interval CLNM = cervical lymph node metastasis FVPTC = follicular variant papillary thyroid carcinoma HR = hazard ratio KM = Kaplan-Meier NCDB = National Cancer Data Base OS = overall survival PTC = papillary thyroid carcinoma RAI = radioactive iodine.

Erken / Geç I-131 Uygulaması

Clin Endocrinol (Oxf). 2014 Mar;80(3):459-63. doi: 10.1111/cen.12301. Epub 2013 Aug 21.

Impact of early vs late postoperative radioiodine remnant ablation on final outcome in patients with low-risk well-differentiated thyroid cancer.

Tsirona S¹, Vlassopoulou V, Tzanela M, Rondogianni P, Ioannidis G, Vassilopoulos C, Botoula E, Trivizas P, Datseris I, Tsagarakis S.

⊕ Author information

Abstract

OBJECTIVE: Postoperative radioiodine remnant ablation (RRA) represents an adjunctive therapeutic modality in patients with differentiated thyroid cancer (DTC). The impact of late vs early RRA on the outcome of DTC is currently unclear. The aim of the study was to evaluate the outcome of patients with DTC according to RRA timing.

DESIGN RETROSPECTIVE STUDY PATIENTS: A total of 107 TNM stage 1 DTC patients were divided into two groups. In group A (n = 50), RRA was administered in less than 4·7 months median 3·0 (range 0·8-4·7), while in group B (n = 57) in more than 4·7 months median 6 (4·8-30·3) after thyroidectomy. Remission was achieved when stimulated serum Tg levels were undetectable, in the absence of local recurrence or cervical lymph node metastases on the neck ultrasound.

RESULTS: All patients underwent near-total thyroidectomy. The mean age at diagnosis was 49·3 years (range: 18-79 years). There were no statistically significant differences in the histological subtype, the TNM stage, the dose of radioiodine and the time of follow-up, between the two groups. After the RRA treatment, 44 group A patients (88%) were in remission and 6 (12%) in persistence; while in group B, 52 (91·2%) were in remission, 1 (1·8%) in persistence and 4 (7%) in recurrence. At their latest follow-up median 87·3 (23·3-251·6 months), all patients were in remission, either as a result of further iodine radioiodine therapy (in 11 patients) or watchful monitoring.

CONCLUSIONS: The timing of RRA seems to have no effect on the long-term outcome of the disease. Therefore, urgency for radioiodine ablation in patients with low-risk thyroid cancer is not recommended.

Erken / Geç I-131 Uygulaması

Am Surg. 2016 Sep;82(9):807-14.

Timing of Adjuvant Radioactive Iodine Therapy Does Not Affect Overall Survival in Low- and Intermediate-Risk Papillary Thyroid Carcinoma.

Suman P¹, Wang CH, Moo-Young TA, Prinz RA, Winchester DJ.

⊕ Author information

Abstract

There is no consensus regarding the timing of adjuvant radioactive iodine therapy (RAI) therapy in low- and intermediate-risk papillary thyroid carcinoma (PTC). We analyzed the impact of adjuvant RAI on overall survival (OS) in low- and intermediate-risk PTC. The National Cancer Data Base was queried from 2004 to 2011 for pN0M0 PTC patients having near/subtotal or total thyroidectomy and adjuvant RAI. Tumors ≤ 1 cm with negative margins were low risk while 1.1- to 4-cm tumors with negative margins or ≤ 1 cm with microscopic margins were termed intermediate risk. RAI in ≤ 3 months and between 3 and 12 months was termed as early and delayed, respectively. Survival analysis was performed after adjusting for patient and tumor-related variables. There were 7,306 low-risk and 16,609 intermediate-risk patients. Seventeen per cent low-risk and 15 per cent intermediate-risk patients had delayed RAI. Kaplan-Meier analysis did not show a difference in OS for early versus delayed RAI administration in low- (10-year OS 94.5% vs 94%, $P = 0.627$) or intermediate-risk (10-year OS 95.3% vs 95.9%, $P = 0.944$) patients. In adjusted survival analysis, RAI timing did not affect OS in all patients (hazard ratios = 0.98, 95% confidence interval = 0.71-1.34, $P = 0.887$). In conclusion, the timing of postthyroidectomy adjuvant RAI therapy does not affect OS in low- or intermediate-risk PTC.

Kime İyot Verelim ?

- Cerrahın deneyimi nedir ?
- Merkezin/ekibin deneyimi nedir?
- Santral diseksiyon yapılmış mı?
- Lenf nodu değerlendirmesi doğru mu ?
- Gerçek histopatoloji nedir ?
- Rezidüel tiroid dokusu ne kadar ?
- Takip nasıl yapılacak ?
- Postoperatif Tg düzeyi nedir ?
- Tg antikoru pozitif mi?
- Ekipte US konusunda özelleşmiş birisi var mı?

Kime İyot Verelim ?

- Radyoaktif iyot kullanımına ilişkin hala yanıtlanmamış pek çok soru mevcuttur
- Radyoaktif iyot kullanımının tümör boyutuna indirgenmesi pek çok nedenle yanlış olabilir
- Tedavi ve ablasyon amaçlı iyot kullanımı farklı değerlendirilmeli
- Yüksek risk grubunda ve seçilmiş orta risk grubunda iyot kullanımı devam etmektedir
- Bu grupta iyot yan etkilerini tartışmak yersizdir

Kime İyot Verelim ?

- Ablatif amaçlı iyot kullanımı tartışmalıdır
- Düşük risk grubu çoğu zaman cerrahi olarak kür olabilir
- Düşük risk grubunda izlem ve lobektomi tercihi başlıca sonografiye dayalı bir tercihtir
- Düşük risk grubunda ablasyon kullanımı uygun koşullarda azaltılabilir

Kime İyot Verelim ?

- Ablatif iyot kullanımında merkezin izlem stratejisi önemlidir
 - Sonografi
 - Stimüle/suprese Tg ölçümü
 - I-131 tüm vücut tarama
- Sonografik deneyimin düşük olduğu merkezlerde takip kolaylığı önemli bir avantajdır
- Ablasyon uygulama tercihi merkez koşullarına göre değişebilir
- Ablatif amaçlı iyot kullanımında tercih düşük doz (30 mCi)
- Düşük doz ablasyonda iyot yan etkileri daha önemsiz

Sonuç ve öneriler

Düşük risk grubu Total tiroidektomi Postoperatif Boyun US normal

- Tg Ab negatif
- Santral nodal metastaz yok
 - Supresyon/replasman altında postop 4-6. haftada
 - Tg <0.2 ng/mL
 - Tg >0.3 ng/mL

- Tg Ab negatif
- Santral nodal metastaz var
 - 3 hafta T4
 - 3 hafta T4 stop
 - Postop 6. haftada
 - Tg <0.2 ng/mL
 - Tg >0.3 ng/mL

- Tg Ab pozitif
- Santral nodal metastaz var
 - Ablasyon
- Santral nodal metastaz yok
 - Supresyon/replasman altında Tg-Ab takibi, azalmıyorsa ablasyon

Sonuç ve öneriler

Orta risk grubu
Total tiroidektomi $\pm$ LND
Postoperatif Boyun US normal

- Tg Ab negatif
- Postop 6. haftada stimüle Tg
 - Tg < 0.2 ng/mL izlem
 - Tg 0.3 – 10 ng/mL 30 mCi
 - Tg > 10 ng/mL $\geq$ 100 mCi

- Tg Ab pozitif
- 30 mCi ablasyon
- Tg-Ab takibi gerekirse ek tedavi

Sonuç ve öneriler

Yüksek risk grubu Total tiroidektomi $\pm$ LND

- Tg Ab negatif
- Postop 6. haftada stimüle Tg
 - Tg 0.3 – 10 ng/mL 30 mCi
 - Tg > 10 ng/mL $\geq$ 150 mCi

- Tg Ab pozitif
- $\geq$ 100 mCi

- İyot pozitif metastatik odak +
 - Cerrahi şansı yoksa
6-12 ay sonra tedavi tekrarı
- İyot negatif metastatik odak +
 - Alternatif tedaviler

İyota Refrakter Tümörler

- İyi diferansiye tümörlerin %5-10'u iyota refrakter ve FDG pozitif hale dönüşebilirler
- İyota refrakter tümörler
 - %50 Az diferansiye tümörler
 - %25 İyi diferansiye tümörler
 - %25 Tall cell varyant
- Anaplastik tümörler

I-131 Negatif Tümörler

- En az 1 kez ideal koşullarda yüksek doz tedavi
 - Uptake yok
 - Tg yanıtı yok
- İdeal koşullar
 - TSH stimülasyonu
 - Düşük iyotlu diyet
 - Lityum

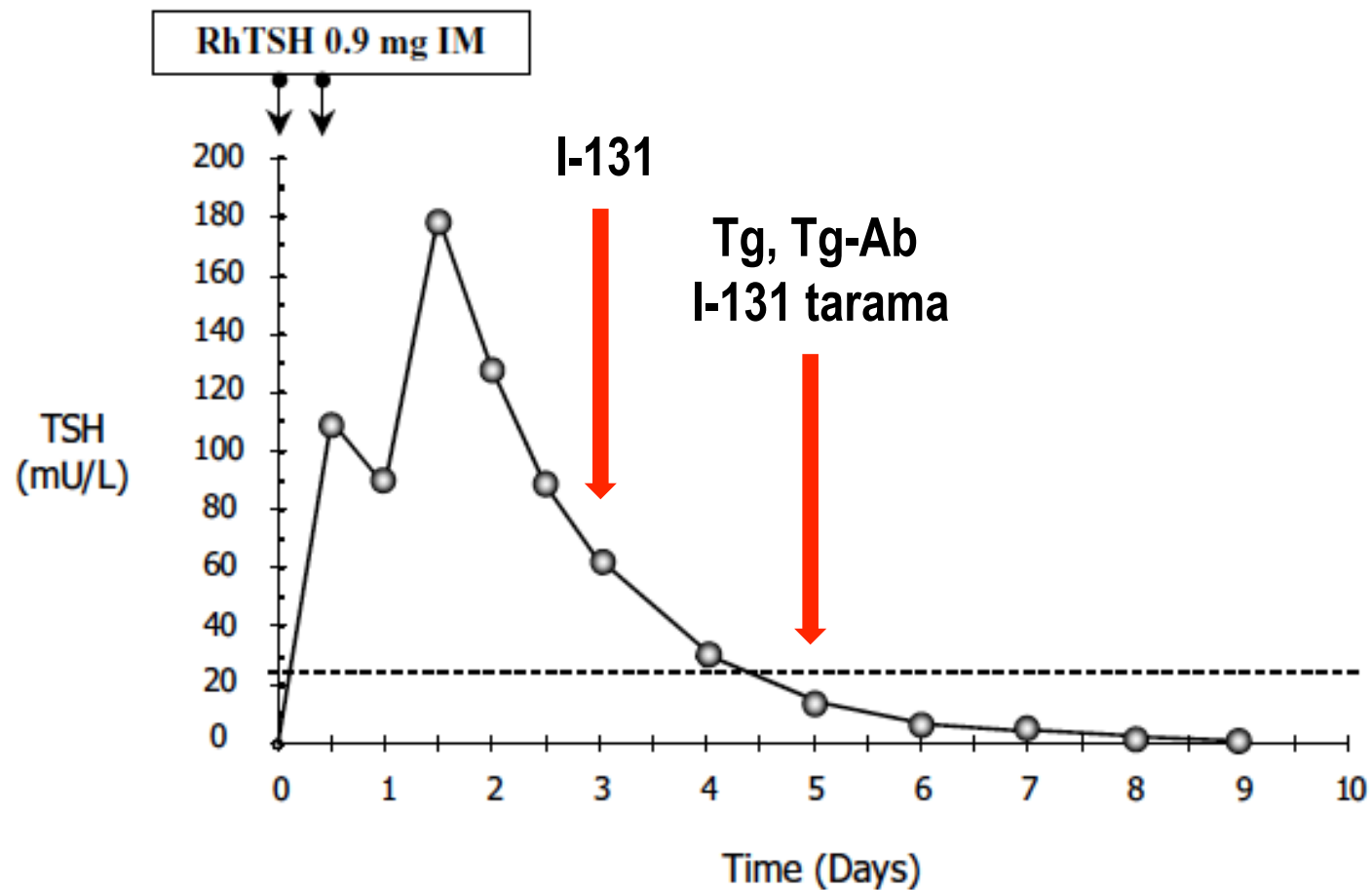
TSH Stimülasyonu

- TSH > 30 μ IU/mL !!
 - Optimal TSH düzeyi için kontrollü çalışma yok
- T4 başlamadan postop 4-6. haftada I-131
- İlk 3 ayda I-131 uygulanması tercih edilir
- Tiroid hormonu başlanmışsa
 - 3-6 hafta T4
 - 2-3 hafta T3
 - Çocuklarda 2 hafta

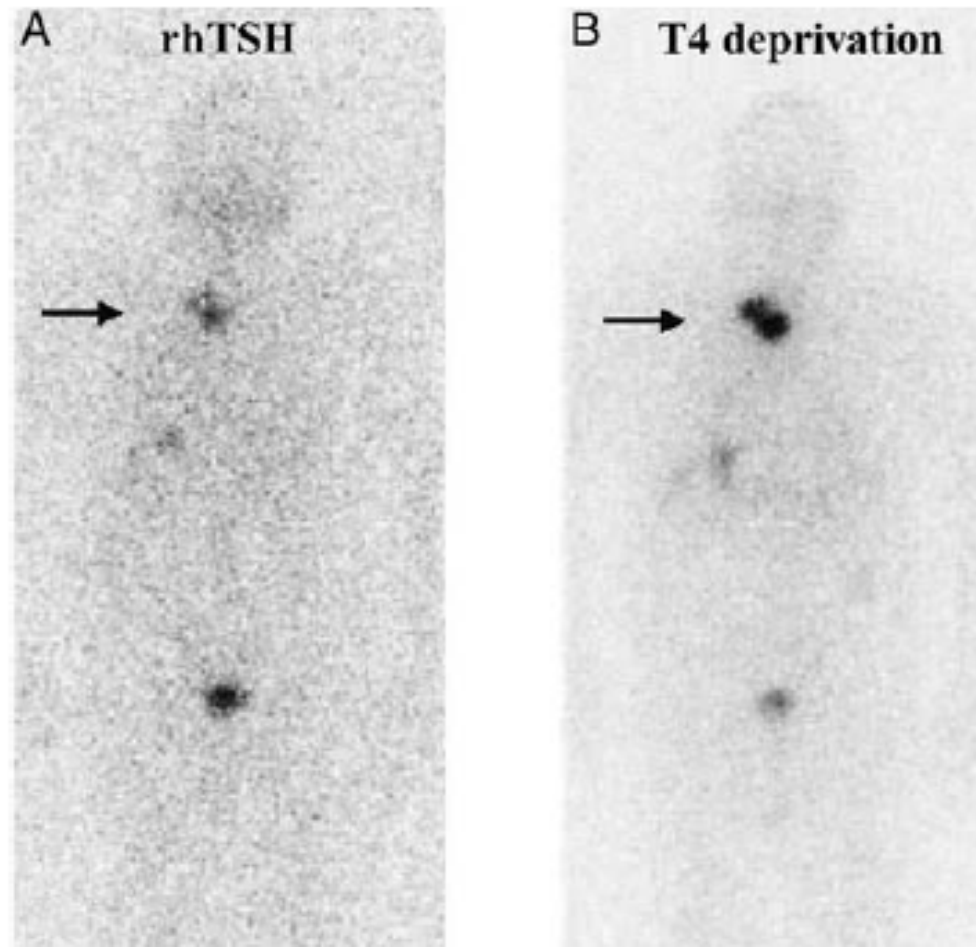
TSH Stimülasyonu

- Ablatif uygulamada Thyrogen kullanılabilir
- Yüksek/orta risk grubunda thyrogen kullanımı tartışmalı
- Thyrogen protokolinde doz kararında stimüle Tg değerleri kullanılamaz

Thyrogen

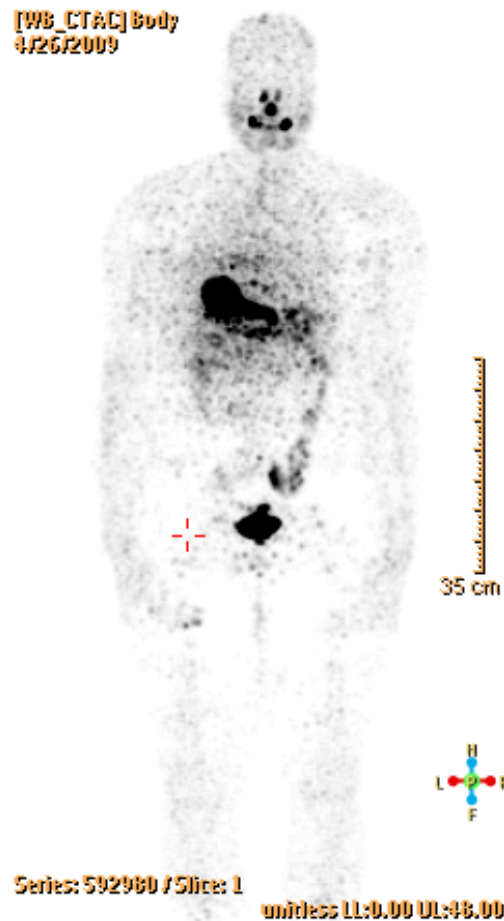


RhTSH vs hTSH

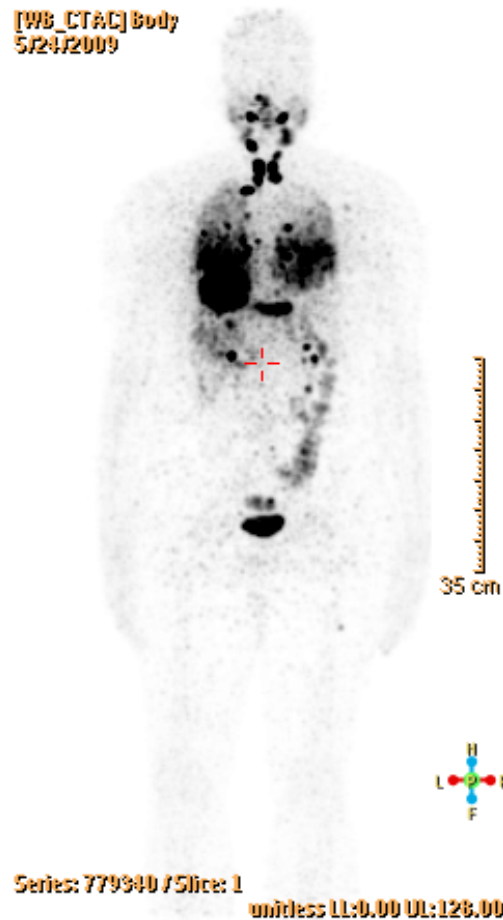


^{124}I PET and the Preparation with THW vs rhTSH

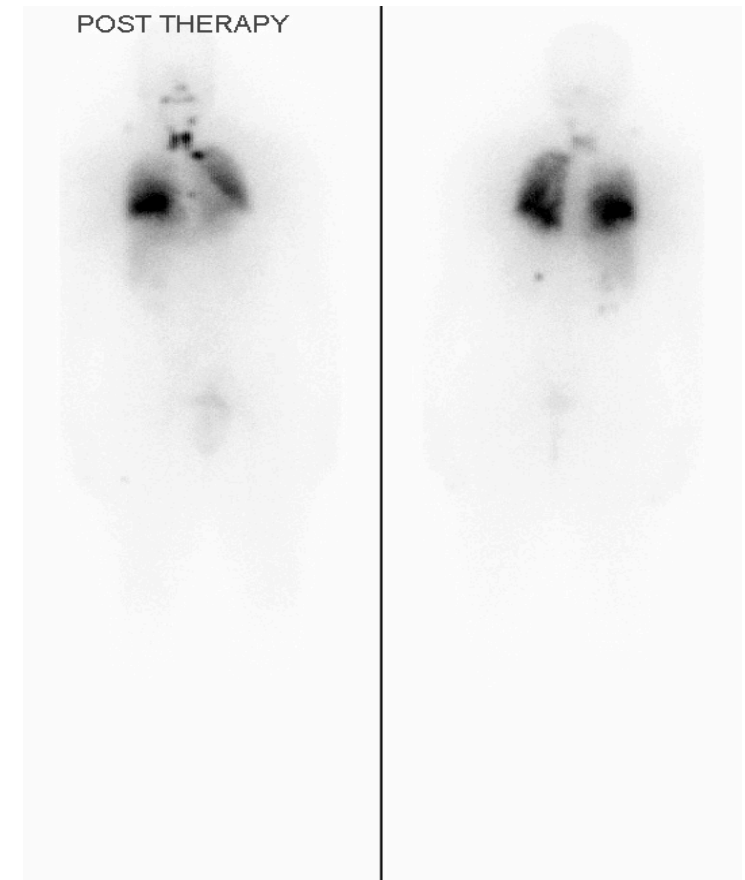
rhTSH



THW



Post-therapy THW



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