RESEARCH ARTICLE / *Araştırma Makalesi*

The Importance of ROLL Tecnique at Surgical Treatment of Paratyroid Adenomas-Our Clinical Experiences

Paratiroid Adenomlarının Cerrahi Tedavisinde "Radioguided Occult Lesion Localization-ROLL" Tekniğinin Önemi-Klinik Tecrübemiz

Fadime Güven[1], Erdem Karadeniz[2], Mustafa Filik[3], Mecit Kantarcı[1]

[1] Atatürk Üniversitesi Tıp Fakültesi Radyoloji A.D.
[2] Atatürk Üniversitesi Tıp Fakültesi Genel Cerahi A.D.
Atatürk Üniversitesi Tıp Fakültesi Nükleer Tıp A.D.

Yazışma Adresi / *Correspondence:*
Fadime Güven

Adnan Menderes Mah. 10. Ara sokak, Erguvan Sitesi No:12 Palandöken/ Erzurum
T: **+90 533 356 71 49** E-mail: **fadimefil@yahoo.com**

Geliş Tarihi / Received : **06.01.2020** Kabul Tarihi / Accepted : **06.03.2020**

Orcid :

Fadime Güven https://orcid.org/0000-0002-9598-8458
Erdem Karadeniz https://orcid.org/0000-0001-6319-1754
Mustafa Filik https://orcid.org/0000-0003-2377-3068
Mecit Kantarcı https://orcid.org/0000-0002-1043-6719

(Sakarya Med J / ***Sakarya Tıp Dergisi*** **2020, 10(1):113-120) Doi: 10.31832/smj.671140**

Çalışma, sözel bildiri olarak 5-10 Kasım 2019 tarihinde Antalya'da yapılan 40. Ulusal Radyoloji Kongresi'nde sunulmuştur.

Abstract

Objective The most important cause of primary hyperparathyroidism (PHP) is parathyroid adenomas. While the reason is mostly the adenomas originating from the parathyroid glands, which are mostly localized around the thyroid gland, ectopic localization can also be seen. The gold standard is surgical excision of adenoma. One of the most important factors affecting surgical success is the correct localization of adenoma preoperatively. Our aim is to investigate the contribution of ROLL technique to the surgical treatment of parathyroid adenomas.

Materials and Methods 40 cases, which were directed due to clinic and laboratory data or incidentally detected, clearly localized preoperatively with ultrasonography (US) and/or scintigraphy findings and surgically excised using ROLL technique between November 2017 and October 2019 were included in the study. Cases where could not be clearly localized preoperatively on US were excluded from the study. The preoperative and postoperative PTH (parathyroid hormone) and Ca (calcium) values were analyzed retrospectively.

Results Postoperative PTH and Ca values were found to decrease in all cases. Histopathological results were confirmed as parathyroid adenoma. In cases, which were operated by using ROLL technique, the duration of the operation was significantly reduced and therefore shorter anesthesia and earlier hospital discharge were provided.
PTH values were found to be increased only in 3 cases in postoperative controls, and no other problems were detected in the follow-ups of other cases.

Conclusions In surgical excision of parathyroid adenoma, the ROLL technique is a safe adjuvant method that can contribute positively to the duration and process of treatment.

Keywords parathyroid adenoma; ultrasonography; minimally invasive parathyroidectomy

Öz

Amaç *Primer hiperparatiroidizmin (PHP) en önemli nedeni paratiroid adenomlarıdır. Sebep, çoğunlukla tiroid bezi çevresinde yerleşmiş paratiroid bezlerinden kaynaklanan adenomlar olmakla birlikte daha nadir olarak ektopik yerleşim de görülebilmektedir. Tedavide altın standart cerrahi olarak adenomun eksizyonudur. Cerrahi başarıyı etkileyen en önemli faktörlerden birisi ise preoperatif olarak adenomun doğru olarak lokalize edilebilmesidir. Bu çalışmada amaç, ROLL tekniğinin paratiroid adenomlarının cerrahi tedavisinde tedaviye katkısını araştırmaktır.*

Gereç ve Yöntemler *Çalışmaya Kasım 2017 ile Ekim 2019 yılları arasında, klinik ve laboratuvar verileri nedeniyle yönlendirilen veya insidental olarak saptanan, ultrasonografi ve/veya sintigrafi bulgularıyla preoperatif olarak net olarak lokalize edilen ve ROLL tekniği kullanılarak cerrahi eksizyon yapılan 40 olgu dahil edilmiştir. Herhangi bir nedenle ROLL tekniği uygulanamayan veya ultrasonografide preoperatif net olarak lokalize edilemeyen olgular çalışma dışı bırakılmıştır. Çalışmaya dahil edilen tüm olgulara ait preoperatif ve postoperatif PTH (parathormon) ve Ca (kalsiyum) değerleri retrospektif olarak incelenerek ROLL tekniğinin tedavi sürecine katkısı araştırılmıştır.*

Bulgular *Çalışmaya dahil edilen tüm olgularda postoperatif PTH ve Ca değerlerinde anlamlı düşüş olduğu saptandı. Tüm olguların histopatolojik sonucu paratiroid adenomu olarak teyit edildi. ROLL tekniği uygulanarak operasyon yapılan olgularda operasyon süresi anlamlı olarak azalmış olup bu nedenle daha kısa anestezi ve daha erken hastane çıkışı sağlanmıştır. Postoperatif kontrollerde yalnızca 3 olguda PTH değerlerinde yükselme saptanmış olup diğer olgularda takipte herhangi bir problem saptanmamıştır.*

Sonuç *Paratiroid adenomunun cerrahi eksizyonunda ROLL tekniği, tedavi süresine ve sürecine olumlu katkılar sağlayabilen, güvenli yardımcı bir yöntemdir.*

Anahtar Kelimeler *paratiroid adenomu; ultrasonografi; minimal invaziv paratiroidektomi*

Introduction

Primary hyperparathyroidism (PHPT) is the most common cause of benign hypercalcemia. The disease is characterized by excessive PTH release from the parathyroid glands. While the reason for approximately 80-85% of the cases is sporadic and single parathyroid adenoma, it is followed by parathyroid hyperplasia, double adenomas and more rarely parathyroid carcinomas.[1] The main treatment method is surgical excision of the adenoma.

While bilateral neck exploration based on the principle of monitoring all parathyroid glands is still a valid technique today, unilaterally limited surgical approach [minimally invasive parathyroidectomy (MIP)] has become more widely accepted in single adenomas, which are detected as the etiologic factor in the majority of cases. Studies have shown that the surgical success of MIP is similar to that of bilateral neck exploration, it further shortens the duration of operation and hospital stay, reduces costs and reduces the incidence of complications such as transient hypocalcemia. [2,3]

Although MIP has equal healing rates with bilateral neck exploration, it has been shown with the studies that it contributes to the reduction of surgery duration, reduction of hospitalization duration and costs.[4,5]

However, it should be kept in mind that the surgical success of MIP is closely related to the accurate determination of the presence of adenoma by preoperative imaging methods. Dual-phase parathyroid scintigraphy with high resolution US and Tc-99m MIBI are the most used and most sensitive imaging methods for localizing the presence of preoperative adenoma. The presence of parathyroid adenoma can be detected at a high rate such as (> 95%), especially when the results of these two methods are compatible.

The localization technique called "Radioguided occult lesion localization (ROLL)" is a new marking technique performed using gamma surgical probe. The ROLL technique, which, today, is also used for excisional biopsy of non-palpable breast masses, is based on the direct injection of radioactive particles such as Tc-99m-labeled macroaggregated albumin (MAA) or colloid into the lesion guided by monitoring methods. The ROLL technique is a promising method that has recently been used in non-palpable nodal recurrences and parathyroid adenomas in thyroid cancers.[6]

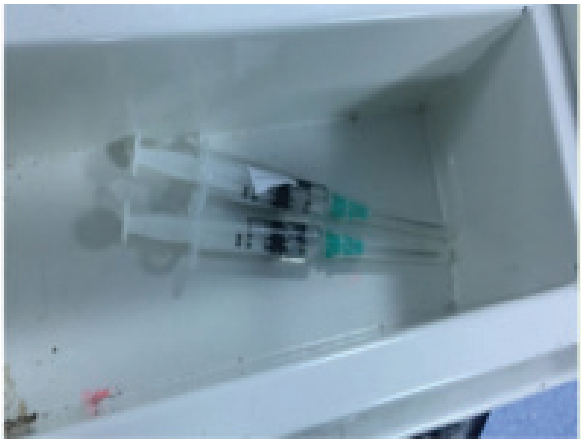
In this study, our aim is to investigate the contribution of this technique to the treatment process in cases of parathyroid adenoma operated by the ROLL technique in Atatürk University Medical Faculty Research Hospital.

Materials And Methods

Our study has planned as a descriptive study/case series. 40 cases operated in our center by ROLL technique due to parathyroid adenoma between November 2017 and October 2019 were included in the study. Cases where could not be clearly localized preoperatively on US or operated without ROLL technique, were excluded from the study. The age range of the patients was between 18-75 (mean 47,6±13,213). 36 of the cases were female (90 %) and 4 of them were male (10 %). In all cases, parathyroid adenoma was localized and reported preoperatively by US and/or scintigraphy. After the patient was taken to the operating table, MAA (macroaggregated albumin) (figure 1) prepared by the Nuclear Medicine department was injected together with 1-2 dizyem, 0.2 mCi US by a radiologist (Fadime Güven-FG) into the lesion compatible with parathyroid adenoma (figure 2). The lesion was then surgically removed using gamma probe (figure 3). Following the excision, it was confirmed that the lesion, which was removed with the aid of gamma probe, was the pre-operatively marked lesion.

The study was approved by the ethics committee of Ataturk Univercity Medical Faculty by the date of 26.12.2019. The protocol number of ethics committee is B.30.2.A-

TA.0.01.00/560. And our study was conducted in accordance with the Helsinki Declaration.



Figüre 1. MAA (macroaggregated albumin) prepared by the Nuclear Medicine department.

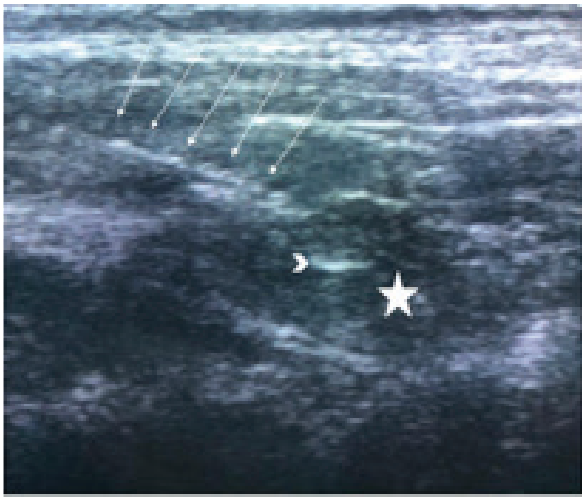


Figure 2. At ultrasound guided (arrows) MAA injected into the lesion compatible with parathyroid adenoma (star) . Note the hyperechoic needle tip at the center of the lesion during injection (arrowhead). After injection of 99mTc macroaggregated albumin, the border of the adenoma blurred because of microbubbles within the radiopharmaceutical.

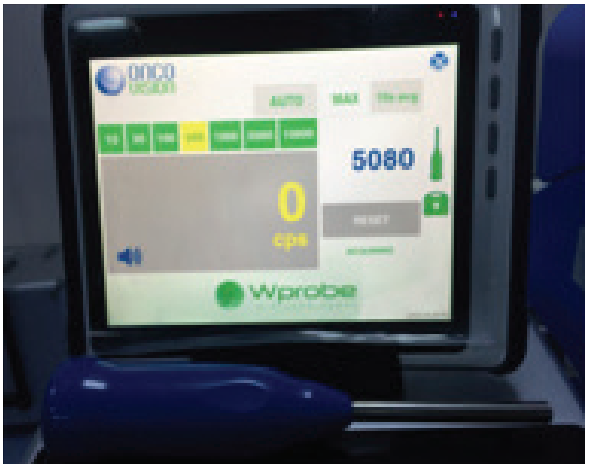


Figure 3. Gamma probe used during surgery

Results

In all 40 cases, parathyroid adenoma was localized on US (figure 4) while in 31 cases, scintigraphy and US findings were supporting each other (figure 5).

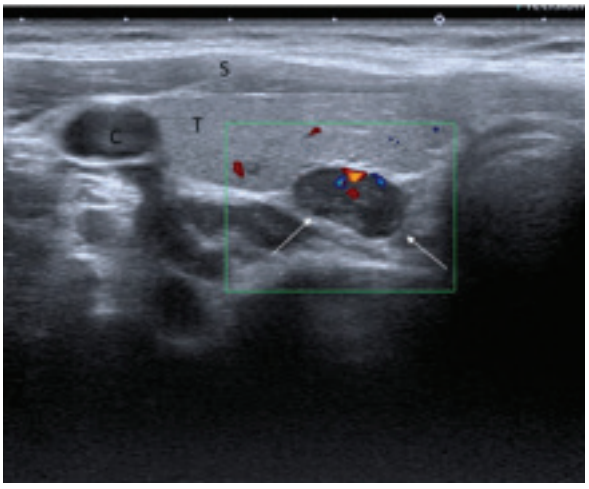


Figure 4. Axial US slice of the right thyroid lobe. Markedly hypoechoic solid lesion that peripherally vascular typical extrathyroidal location for parathyroid adenoma (arrows). C: right common carotid artery, S: strap muscles, T: right thyroid lobe.

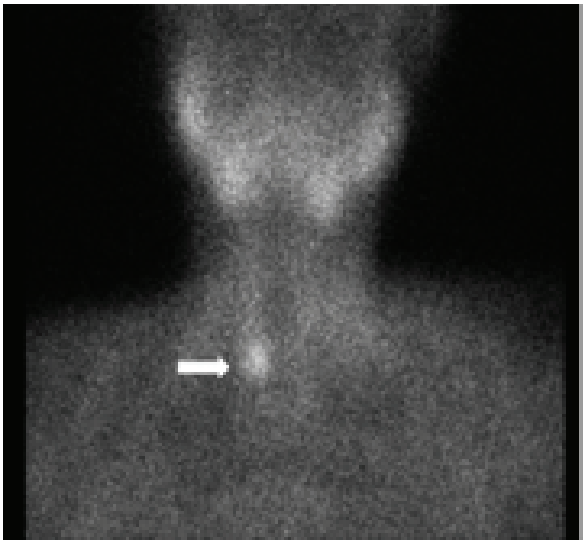


Figure 5. 99mTc-MIBI shows slightly increased retention of radiotracer compatible with right inferior parathyroid adenoma (arrow).

MIBI scintigraphy was reported to be negative in 9 cases (table 1). The tissues removed during surgery were confirmed to be pre-operatively marked lesions with the aid of a gamma probe (figure 6).

Figure 6. The tissues removed during surgery were confirmed to be pre-operatively marked lesions with the aid of a gamma probe (a, b).

In all cases, PTH and Ca values were found to be decreased in the control analyses made after 24 hours (table 1). The presence of parathyroid adenoma was also confirmed histopathologically in all cases. Therefore, the success rate was accepted as 100%. In our case group, while no abnormalities were detected in PTH and serum Ca levels in 37 cases in the follow-up, in 3 cases, PTH values were increased while Ca values were within normal limits. We believe that the reason for the increase in PTH values in these cases may be a millimetric-sized second adenoma, which we could not detect preoperatively.

Another important advantage of the technique was that it significantly reduced the duration of the operation as targeted treatment was performed. While the operation time was between 15-35 minutes in our case group, it is stated by experienced surgeons in this particular field that in parathyroid surgeries performed without using ROLL technique, this period generally varies between 45 and 60 minutes. The fact that the surgical operation performed with this technique is relatively less invasive will undoubtedly reduce post-operative complications and the length of hospital stay. Confirmation of the removed tissue with the aid of gamma probe also minimizes the possibility of insufficient surgery. However, the point that should be kept in mind is that the interventional procedures that guide the treatment should be performed by experts with sufficient experience in the diagnosis and treatment phase.

Table 1. Preoperative characteristics and pre-postoperative parathotmon and calcium levels of patients undergoing radioguided occult lesion localization-guided minimally invasive parathyroidectomy

Patient number	Sex/age (years)	Location of adenoma	Adenoma size on US(mm)	MIBI scintigraphy	*Surgery time (min)	Pre-op PTH	Post-op PTH	Pre-op Ca	Post-op Ca
1	F/50	LI	7x4	negative	20	128	75	10,5	9,7
2	F/71	RI	7x8	positive	35	141	14	12,3	8,3
3	F/56	LI	8x6	negative	30	202	13	12	8,3
4	F/53	LI	9x6	positive	20	147	3	11,9	8,5
5	F/35	RI	7x4	positive	15	115	17	11,3	8,4
6	F/54	LI	11x7	positive	17	90	71	11,9	8,6
7	F/75	LI	22x12	positive	18	190	6	11,1	9,5
8	F/57	LI	18x7	positive	15	185	18	11,5	9,1
9	F/63	LI	10x5	positive	20	92	8	12,1	9
10	F/54	LS	11x7	positive	17	147	18	11,9	8,3
11	F/53	LI	6x5	negative	23	121	3	11	9
12	F/65	RI	16x10	positive	15	206	30	11,6	9,1
13	F/61	LI	9x4	positive	35	115	5	10,5	8
14	F/57	RI	5x5	negative	22	149	11	10,7	8,5
15	F/33	LI	8x4	negative	25	299	21	11,1	8,4
16	F/51	LI	12x7	positive	17	255	20	12	9,5
17	F/36	LI	11x8	positive	25	211	54	10,7	8,5
18	F/46	LI	8x7	positive	30	185	34	10,6	8,6
19	M/53	LI	7x4	positive	25	122	10	11,2	8,3
20	F/41	RI	8x5	positive	25	188	44	10,5	8,3
21	F/27	RI	18x12	positive	15	407	6	10,5	7,6
22	F/42	RS	9x6	positive	15	195	42	11,6	8,7
23	F/58	LI	13x8	positive	25	261	36	11	8,4
24	F/56	LI	6x4	positive	15	110	25	11	8,6
25	F/53	RI	10x8	positive	22	108	36	10,1	8,1
26	F/28	RI	13x7	positive	18	156	49	10,4	9
27	F/43	RI	11x5	positive	30	146	53	9,1	8,5
28	M/38	RI	11x9	positive	35	146	50	11,5	8,7
29	F/43	LI	8x5	positive	15	202	49	11	8,3
30	F/56	LI	8x4	negative	20	115	55	11,6	8,7
31	F/47	LI	7x4	positive	22	95	34	10,3	8,1
32	F/26	LI	12x9	positive	20	254	60	10,8	8,8
33	F/39	RI	11x6	positive	18	105	37	10,3	9
34	M/18	RI	12x10	positive	30	176	68	10,8	8,5
35	F/55	RI	11x9	negative	25	216	10	12,8	9
36	M/23	LI	10x8	positive	30	143	9	12,1	8,5
37	F/51	LI	9x7	negative	20	137	44	11,1	10
38	F/60	RI	16x11	positive	25	114	42	10,9	7,2
39	F/47	LI	14x5	negative	23	251	9	11	8,6
40	F/30	LI	10x6	positive	15	157	64	9,9	9,3

F: female, M: male, RI: right inferior, LI: left inferior, RS: right süperior, LS: left süperior
* Time from incision to excision of adenoma.

Discussion

PHPT refers to the clinical picture due to hypersecretion of PTH. Its most common cause is single parathyroid adenomas (85%). Parathyroid hyperplasias (12%), multiple adenomas (5%) and rarely parathyroid carcinomas (1%) are the etiologic factors. The gold standard in treatment is still surgical excision of adenoma. To this end, the use of the MIP technique, which has been increasing in recent times, remains up to date. MIP technique was first described by Tibblin. [7] An important point to keep in mind is that one of the most important factors that increase the surgical success rate of MIP technique is the effective and correct use of preoperative imaging techniques. The most preferred imaging methods for preoperative lesion localization are US performed by experienced radiologists and Tc-99m MIBI scintigraphy performed by the nuclear medicine department. In the combined imaging where these two methods are used together, probability of correct localization of the lesion is quite high (sensitivity was reported as 96%, specificity as 83%, positive predictive value as 88% and negative predictive value as 94%).[8]

The most popular method of assisted surgical techniques in MIP is the use of gamma surgical probe. Since the method depends on the accumulation of radioactive material in parathyroid adenomas compared to the surrounding tissues, the use of gamma surgical probe requires the parathyroid adenoma to be scintigraphically positive. Therefore, it is not beneficial to use this technique in cases that are scintigraphically negative.[6]

In the ROLL technique, which has been defined for the same purpose and recently used, the detection of lesion independent of Tc99m MIBI retention capability is concerned. In this case, injection of radioactive material, with much lower doses, into the lesion is performed compared to IV application with the imaging methods (US). In the ROLL technique, the excision of the lesion with the aid of gamma probe after US guided radioactive material injection is much easier. The presence of background activity in surrounding tissues other than adenoma in IV application may make it difficult to find the lesion. However, the ROLL method is a local application; since there is activity only in the injection areas in the surgical region, there will be no involvement of radioactivity in other regions, which will make surgery easier and faster. Another advantage of the ROLL technique is that it can contribute to the optimal determination of the incision level by localizing the lesion on the skin before the incision.[6]

In patients without ROLL technique, approximately 4 cm of incision is required, whereas only 2 cm of incision is sufficient for operation with this technique. In our case group, the incision size was reduced by 50% and better cosmetic results were achieved.

We noticed that in patients without ROLL technique, about 2 days hospitalization is required, whereas only 1 day is sufficient for discharge with this tecnique, generally. This technique also reduces hospitalization by up to 50%, too.

The most important condition for the effective application of the ROLL method is that the lesion can be monitored by US and it is in the proper location to inject radioactive material under US guidance. Especially in the US examination performed by experienced users, localization of the lesion and imaging-guided interventional procedures can be performed effectively. In addition, the ROLL method provides a significant contribution to the correct localization of the lesion, especially in recurrent cases with minimal invasive approach.

In our case group, radioactive material was injected to all cases by an experienced radiologist (FG) in this particular subject, with US guidance in the operating room. Surgical excision of the lesions was achieved faster and more effectively with the help of gamma probe.

The ROLL technique has several disadvantages as well as

the advantages mentioned. The most important of these is that the lesion is in suitable localization for US-guided intervention. In addition, since the surgeon can reach the lesion by following the radioactivity in the ROLL technique, it is of most importance that the injection is performed with the correct technique and into the lesion. For this reason, it is important to have a team member experienced in US-guided interventions and working with radioactivity in the centers where the technique is applied. Even with due diligence, there might be reflux through the needle line of the activity injected especially into small lesions.[6]

In case of leakage of radioactivity outside the lesion, it may cause counting with gamma probe after excision of the lesion in adjacent soft tissues. However, the obtained counting rate in the lesion is very high compared to the lesion bed. Since the main objective of this technique is to direct the surgeon to the right lesion, presence of minor leakage to the surrounding tissue does not make it difficult to find the lesions.[9]

Surgical treatment in PHPT provides high rates of successful results, but persistent or recurrent diseases can also be seen. The highest persistent/recurrent PHPT rates were reported in double adenomas. In a large series, persistent disease rates in double adenoma, single adenoma and hyperplasia have been reported as 4%, 1.3% and 2.2%, respectively. Similarly, recurrence rates were found to be 7.3%, 1.7% and 4.4%, respectively.[1o] In our case group, there is a possibility of the presence of a second adenoma that could not be detected preoperatively in 3 cases, where an increase was observed in PTH levels again in the follow-up.

The most important factor affecting surgical success in parathyroid adenomas is the correct localization of the lesion preoperatively. The presence of double adenoma may not be detected preoperatively, even if necessary care is taken. This is one of the most important causes of recurrence in parathyroid surgery.

The ROLL technique is one of the promising assisting techniques that was started to be used in primary parathyroid surgery. The effective use of the ROLL technique can be an important contribution to the surgical success, especially in lesions smaller than 1 cm and in the surgery of recurrent cases, the morbidity of which are higher due to fibrosis caused by previous surgery.

The study was approved by the ethics committee of Ataturk Univercity Medical Faculty by the date of 26.12.2019. The protocol number of ethics committee is B.30.2.ATA.0.01.00/560. And our study was conducted in accordance with the Helsinki Declaration.

References

1. *Gopalakrishna Iyer N, Shaha AR. Current concepts in the management of primary hyperparathyroidism. Indian J Surg Oncol 2010; 1(2):112-9.*
2. *Goldstein RE, Blevins L, Delbeke D, Martin WH. Effect of minimally invasive radioguided parathyroidectomy on efficacy, length of stay, and costs in the management of primary hyperparathyroidism. Ann Surg 2000; 231(5): 732-42.*
3. *Bergenfelz A, Lindblom P, Tibblin S, Westerdahl J. Unilateral versus bilateral neck exploration for primary hyperparathyroidism: a prospective randomized controlled trial. Ann Surg 2002;236(5):543-51.*
4. *Goldstein RE, Blevins L, Delbeke D, Martin WH. Effect of minimally invasive radioguided parathyroidectomy on efficacy, length of stay, and costs in the management of primary hyperparathyroidism. Ann Surg 2000; 231:732–742.*
5. *Bergenfelz A, Lindblom P, Tibblin S, Westerdahl J. Unilateral versus bilateral neck exploration for primary hyperparathyroidism: a prospective randomized controlled trial. Ann Surg 2002; 236:543–551.*
6. *Aydın OU, Küçükel F, Soylu L, Aydın S, Sengezer T, Ilgan S. The Use of ROLL Technique in Recurrent Hyperparathyroidism Due to Double Parathyroid Adenoma: Case Report. Turkiye Klinikleri J Endocrin 2015;10(1):31-5.*
7. *Tibblin S, Bondeson AG, Ljungberg O. Unilateral parathyroidectomy in hyperparathyroidism due to single adenoma. Ann Surg 1982; 195(3):245-52.*
8. *Aliyev A, Kabasakal L, Simsek O, Paksoy M, Halac M, Uslu I. Ectopic parathyroid adenoma localized with MIBI scintigraphy and excised with guide of macroaggregated human serum albumin injection. Clin Nucl Med 2010;35(3): 151-3.*
9. *Ilgan S, Ozbaş S, Bilezikci B, Sengezer T, Aydın OU, Gursoy A, et al. Radioguided lesion ocalization for minimally invasive parathyroidectomy: technical consideration and feasibility. Nucl Med Commun 2014;35(11):1167-74.*
10. *Alhefdhi A, Scheider DF, Sipper R, Chen H. Recurrent and persistence primary hyperparathyroidism occurs more frequently in patients with double adenomas. J Surg Res 2014;190(1):198-202.*