INTRAOPERATIVNI ULTRAZVUK U LOKALIZOVANJU NEPALPABILNIH LEZIJA DOJKE

SERIJA SLUČAJEVA

CASE SERIES

INTRAOPERATIVE ULTRASOUND IN LOCALIZING NONPALPABLE BREAST LESIONS

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SAŽETAK

Uvod: Intraoperativni ultrazvuk u hirurgiji tumora dojke je relativno novi pristup u lokalizovanju nepalpabilnih tumora. Brojne su prednosti ove tehnike u odnosu na mamografsku preoperativnu lokalizaciju žičanom iglom (*wire needle localisation - WNL),* koja predstavlja standardni pristup u lokalizovanju nepalpabilnih lezija dojke. Pokazalo se da operacije tumora dojke vođene ultrazvukom daju manji procenat pozitivnih ivica resekcije, uz manji volumen ekscidiranog zdravog tkiva dojke oko tumora.

Cilj: Cilj ovog rada je procena uspešnosti ekscizije nepalpabilnih lezija u dojci lokalizovanjem tih lezija intraoperativnim ultrazvukom.

Materijal i metode: Analiza je retrospektivna, obuhvata pacijente operisane na Odeljenju onkološke hirurgije KBC „Bežanijska kosa" u periodu od januara 2013. do decembra 2017. godine. Inkluzioni kriterijum je nepalpabilna lezija kod koje je intraoperativni ultrazvuk bio jedino sredstvo lokalizovanja. Procena uspešnosti identifikovanja i ekscizije nepalpabilnih lezija izražena je u procentima (namera/uspešna realizacija).

Rezultati: Od 2627 pacijentkinja operisanih u ovom periodu, 317 pacijentkinja (11,9%) je imalo nepalpabilne lezije, od kojih su 173 lokalizovane *WNL*, a 144 intraoperativnim ultrazvukom (IOUZ).

Od 144 pacijentkinje kod kojih su lezije lokalizovane IOUZ, 61 je imalo karcinom dojke, a 83 benigne lezije. Na osnovu operativnih nalaza sve nepalpabilne lezije u dojkama su uspešno lokalizovane intraoperativnim ultrazvukom i ekscidirane (144/144 – 100%).

Zaključak: Intraoperativni ultrazvuk predstavlja optimalno sredstvo lokalizovanja ultrazvukom vidljivih nepalpabilnih lezija u dojci kod kojih je indikovana hirurška ekscizija.

Ključne reči: Intraoperativni ultrazvuk, dojka, nepalpabilna lezija

ABSTRACT

Introduction: Intraoperative ultrasound in breast tumor surgery is a relatively new technique used for localizing nonpalpable breast lesions. This procedure has multiple advantages over wire needle localization (WNL), which is a standard approach to localizing nonpalpable breast lesions. It has been shown that intraoperative application of ultrasound is presented with a decrease in tumor-infiltrated resection margins, and with less excised healthy tissue around the tumor.

Aim: The purpose of this article is to evaluate the success rate of nonpalpable breast lesion excisions by localizing them with intraoperative ultrasound.

Material and methods: This is a retrospective study, which involves patients from the Department of surgical oncology at "Bežanijska kosa" treated in the period between January 2013 and December 2017. Medical records of the patients who were not operated on for nonpalpable breast lesions using intraoperative ultrasound were isolated. Success rate of identifying and excising nonpalpable lesions is presented in percentages, so this finding can be compared to other published studies.

Results: Of the 2627 patients operated on during this period, 317 (11.9%) patients had nonpalpable lesions, of which 173 were localized by WNL, and 144 were localized by intraoperative ultrasound (IOUS).

Of 144 patients whose lesions were localized by IOUS, 61 patients had breast cancer, while 83 patients had benign lesions. Based on the medical records, all non-palpable lesions were successfully located and excised with intraoperative ultrasound (144/144- 100%).

Conclusion: Intraoperative ultrasound represents an optimal technique for localizing nonpalpable breast lesions that are visible on ultrasound and are an indication for surgical removal.

Keywords: Intra-operative ultrasound, breast, nonpalpable lesion

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UVOD

Primena intraoperativnog ultrazvuka u hirurgiji tumora dojke je relativno nov pristup u ovoj oblasti onkološke hirurgije, sa još uvek nedovoljno precizno definisanim principima tehnike izvođenja. U kliničku praksu je uveden kao tehnika lokalizovanja nepalpabilnih tumora [1-12], i u svim publikovanim studijama pokazao je značajnu efikasnost, uključujući i nedavno obavljene studije [13-15]. Takodje je pokazao i značajne komparativne prednosti u odnosu na *WNL*, koja je još uvek standardni pristup u lokalizovanju nepalpabilnih lezija dojke [3-6,10,12,16,17].

Pored ovih prednosti, pokazalo se i da operacije tumora dojke vođene ultrazvukom imaju manji procenat pozitivnih ivica resekcije, uz manji volumen ekscidiranog zdravog tkiva dojke oko tumora. Ove činjenice dovele su do toga da se poslednjih godina intraoperativni ultrazvuk primenjuje i u hirurgiji palpabilnih tumora [14,18-24], u cilju optimizacije resekcione procedure i prevazilaženja nedostataka klasične palpacijom vođene hirurgije. Palpacijom vođena hirurgija je subjektivna tehnika koja daje i do 41% pozitivnih ivica resekcije [24], a sa druge strane nepotrebno veliki volumen ekscidiranog tkiva. Krekel i saradnici su pokazali u *COBALT trial-u* [24] da intraoperativno korišćenje ultrazvuka kod palpabilnih tumora daje za 15% manje pozitivnih ivica resekcije nego palpacijom vođena hirurgija, uz značajno manji volumen preparata (*specimen*), a što bi trebalo da utiče na bolji estetski rezultat operacije i bolji kvalitet života.

U opisima tehnike primene intraoperativnog ultrazvuka većina autora se oslanja na markiranje projekcije tumora na koži dojke pre početka operacije, a kada je operacija u toku proverava se odnos tumora i okolnog tkiva uvlačenjem sonde u ranu. Po završetku ekscizije ultrazvukom se pregleda preparat *ex vivo*, uz naknadne ekscizije zidova lože tumora, ukoliko je neka od ivica resekcije isuviše blizu ivici tumora.

Hirurški tim KBC „Bežanijska kosa" razvio je originalnu tehniku dodatnog intraoperativnog markiranja nepalpabilnih lezija dojke specijalno konstruisanim iglama [25,26], koje se u leziju uvode intraoperativno pod kontrolom ultrazvuka, i predstavljaju stabilni marker nepalpabilne lezije. Ovim se prevazilaze neke neprecizности i nedostaci standardne tehnike upotrebe intraoperativnog ultrazvuka.

Cilj ovog rada je procena uspešnosti ekscizije nepalpabilnih lezija u dojci lokalizovanjem tih lezija intraoperativnim ultrazvukom.

MATERIJAL I METODE

Analiza je retrospektivna i obuhvata pacijente operisane na Odeljenju onkološke hirurgije KBC „Bežanijska

INTRODUCTION

The use of intraoperative ultrasound in breast tumor surgery is a relatively new approach in this field of surgical oncology, and the principles pertaining to the surgical technique are insufficiently defined. It was introduced into clinical practice as a localization technique for nonpalpable tumors [1-12], and in all published studies, including recently conducted ones, it showed significant efficacy [13-15]. It also appeared to have significant advantages over *WNL,* which is still a standard approach to localizing nonpalpable breast lesions [3-6,10,12,16,17].

Apart from these advantages, ultrasound-guided breast surgery has presented with a decreased rate of positive surgical margins and less excised healthy breast tissue around the tumor. In recent years, this has led to the use of intraoperative ultrasound in surgical management of palpable breast tumors as well [14,18-24], with the aim of optimizing the resection procedure and overcoming the imperfections of classic palpation-guided surgery. Palpation-guided surgery is a subjective technique with up to 41% of positive surgical margins [24], and an unnecessarily large volume of excised tissue. Krekel and colleagues showed in the *COBALT trial* [24] that the use of intraoperative ultrasound in palpable tumors resulted in a 15%-decrease in positive surgical margins compared to palpation-guided surgery, as well as a significantly lower volume of the preparation (*specimen*), which should bring about a better esthetic result and better quality of life.

When describing the intraoperative ultrasound technique, most authors rely on projection-marking on the skin of the breast prior to surgery, and during surgery the relationship between the tumor and the surrounding healthy tissue is checked by inserting a probe in the wound. Upon excision, the specimen is examined *ex vivo* using ultrasound, followed by re-excisions of the walls of tumor bed if any surgical margin is too close to the tumor margin.

The surgical team of the University Hospital Medical Centre "Bežanijska kosa" have developed an original technique of additional intraoperative marking of nonpalpable lesions with specially designed needles [25,26], which are intraoperatively inserted into the lesion under the control of ultrasound being stable markers of a nonpalpable lesion. This is how some inaccuracies and shortcomings of intraoperative ultrasound are overcome.

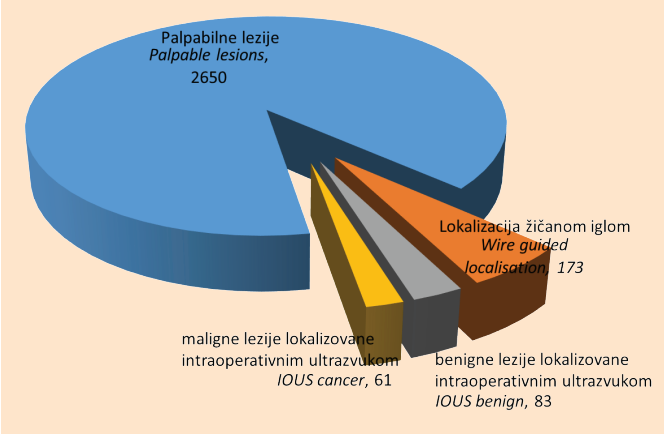
The aim of this paper is to evaluate the success rate of nonpalpable breast lesion excisions by localizing them with intraoperative ultrasound.

kosa“ u periodu od januara 2013. do decembra 2017. godine. Inkluzioni kriterijum je nepalpabilna lezija kod koje je intraoperativni ultrazvuk bio jedino sredstvo lokalizovanja. Procena uspešnosti identifikovanja i ekscizije nepalpabilnih lezija izražena je u procentima (namera/uspešna realizacija).

REZULTATI

U navedenom periodu operisano je 2627 pacijentkinja sa malignim i benignim tumorima dojke. Od toga 317 (11,9%) pacijentkinja je imalo nepalpabilne lezije, od kojih je 173 lokalizovano *WNL („wire needle localisation“)* preoperativnom lokalizacijom na mamografu (većinom su u pitanju mikrokalcifikati, koji se ultrazvukom teško vizualizuju), a 144 intraoperativnim ultrazvukom.

Od 144 pacijentkinje kod kojih su lezije lokalizovane intraoperativnim ultrazvukom 61 je imala karcinom dojke, a 83 benigne lezije. Imajući u vidu da je 6 pacijentkinja imalo dve nepalpabilne lezije, jedna pacijentkinja tri, i jedna četiri nepalpabilne lezije (sve multiple lezije su bile benigne – fibroadenomi), ukupan broj benignih nepalpabilnih lezija je 94 kod 83 pacijentkinje (Prilog I).



Slika 1. Odnos palpabilnih i nepalpabilnih lezija

Figure 1. Ratio of palpable and non-palpable lesions

Na osnovu operativnih nalaza sve nepalpabilne lezije u dojkama su uspešno lokalizovane intraoperativnim ultrazvukom i ekscidirane (144/144 – 100%).

Najmanja lezija bila je promera 4mm (fibroadenom), a najveća 12mm (karcinom – nepalpabilan zbog volumena dojke).

DISKUSIJA

Jedan od najvažnijih pomaka u dijagnostici i lečenju karcinoma dojke poslednjih decenija predstavlja uvođenje skrining programa, koji je u razvijenim zemljama sveta sa visokom incidencom karcinoma dojke iniciran krajem osamdesetih godina XX veka. Efekat skrininga

MATERIAL AND METHODS

A retrospective analysis included patients who were surgically treated at the Department of surgical oncology of the University Hospital Medical Centre “Bežanijska kosa“ in the period between January 2013 and December 2017. The inclusion criterion was a nonpalpable lesion localized only by means of intraoperative ultrasound. The evaluation of successful identification and excisions of nonpalpable lesions is expressed in percentages (intention/successful realization).

RESULTS

During the above-mentioned period, 2627 patients were operated on for malignant and benign breast tumors. A total of 317 (11.9%) patients had nonpalpable lesions out of which 173 were localized with *WNL* (wire needle localization) pre-operatively with the help of mammography (those were mostly microcalcifications that were difficult to visualize with ultrasound), and 144 were localized with intraoperative ultrasound.

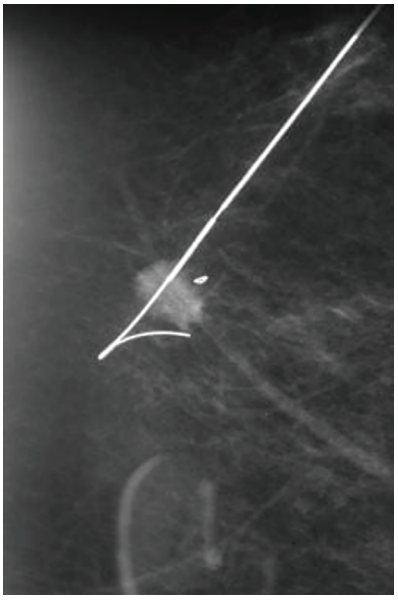
Of the total number of 144 patients whose lesions were localized using intraoperative ultrasound, 61 patients had breast cancer, whereas 83 patients had benign lesions. Considering that there were six patients with two nonpalpable lesions, one patient with three lesions, and one patient with four nonpalpable lesions (all multiple lesions were benign – fibroadenomas), there was a total of 94 benign nonpalpable lesions in 83 patients (Appendix I).

Based on operative findings, all nonpalpable breast lesions were successfully localized using intraoperative ultrasound and then excised (144/144 – 100%).

The smallest lesion was 4mm in diameter (a fibroadenoma), whereas the largest one was 12mm in diameter (nonpalpable carcinoma due to the volume of the breast).

DISCUSSION

The introduction of screening programs, as one of the most important recent achievements, was initiated in developed countries with high cancer incidence at the end of 1980s. The effect of screening on disease control is based on the detection and treatment of a tumor in its early stages, and it is stronger than the effect of any other therapeutic tool developed in the 20th century; breast cancer mortality has been reduced by around 30% in countries with screening programs. Apart from reduced mortality, the detection of tumors in early stages enables surgical treatment with fewer functional and esthetic consequences compared to classical therapeutic procedures, but at the same time it imposes the need to modify classical surgical techniques due

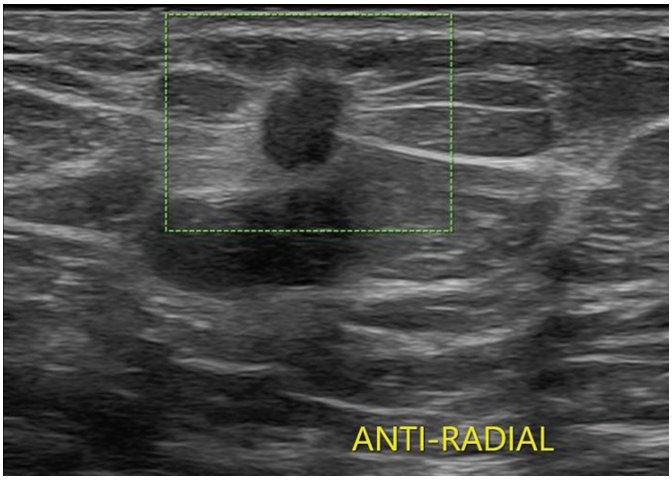


Slika 2. Mamografsko lokalizovanje nepalpabilne lezije žičanom iglom

Figure 2. Mammographic localization of a non-palpable lesion with a wire needle

na kontrolu bolesti je zasnovan na otkrivanju i lečenju tumora u ranijim fazama bolesti, a jači je od bilo kog drugog terapijskog sredstva razvijenog tokom XX veka; za oko 30% je smanjena smrtnost od ove bolesti u zemljama sa skrining programima. Pored smanjene smrtnosti, otkrivanje tumora u ranijim fazama omogućava hirurško lečenje sa manje funkcionalnih i estetskih posledica u odnosu na klasične terapijske procedure, ali u isto vreme nameće potrebu za modifikacijom klasičnih hirurških tehnika zbog otkrivanja proporcionalno većeg broja lezija u dojci koje se zbog malih dimenzija ne palpiraju. Osnovno sredstvo u lokalizovanju i izvodjenju ekscizije lezija dojke u klasičnoj hirurgiji je palpacija.

Hirurgija nepalpabilnih tumora dojke predstavlja novo poglavlje u oblasti hirurgije tumora dojke jer podrazumeva vizualizacionu podršku koju klasična hirurgija ne poznaje. Vizualizacione tehnike koje se koriste u tu svrhu su iste one kojima se tumori dojke dijagnostikuju: mamografija i ultrazvuk. Mamografsko lokalizovanje nepalpabilnih lezija dojke je dominantan pristup, sprovodi se preoperativnim uvodjenjem žičane igle ili radioaktivnog obeleživača u leziju pod kontrolom mamografa, a ti markeri služe hirurgu kao orijentacija u pogledu mestu lezije tokom operacije. Intraoperativni ultrazvuk je mnogo ređe korišćeno sredstvo u lokalizovanju nepalpabilnih lezija u dojci, ali ima značajne komparativne prednosti u odnosu na mamografsko lokalizovanje jer prevazilazi probleme i nedostatke mamografskog (preoperativnog) lokalizovanja: stres pacijentkinje, organizaciono uskladjivanje rada mamografskog kabineta i operacione sale, mogućnost pomeranja markera od trenutka obeležavanja



Slika 3. Ultrazvukom viđen i lokalizovan nepalpabilni tumor dojke

Figure 3. A non-palpable breast tumor seen and localized by ultrasound

to detecting proportionally larger number of breast lesions which are nonpalpable because of small dimensions. Palpation is the basic means of localizing and performing breast lesion excisions in classical surgery.

Nonpalpable breast tumor surgery is a new chapter in the field of breast tumor surgery as it involves visualization support unknown to classical surgery. Visualization techniques used for this purpose are the same techniques that are used for diagnosing breast cancer: mammography and ultrasound. Mammographic localization of nonpalpable breast lesions is a dominant approach, it is carried out by preoperatively introducing a wire needle or a radiographic marker into the lesion during mammography, and surgeons use these markers as orientation regarding the location of the lesion during surgery. Intraoperative ultrasound is less frequently used for localizing nonpalpable breast lesions, but it has significant advantages over mammographic localization as it overcomes the problems and imperfections of mammographic (preoperative) localization: in-hospital stress, coordinating the activities in the mammography room and the ones in the operating theatre, the possibility of marker-migration from the moment of marking to the moment of surgery. The only limitations regarding the application of ultrasound are associated with the surgeon's knowledge and the availability of an ultrasound in the operating theatre, as well as lesions that are not ultrasound-visible.

In this study, we analyzed the use of intraoperative ultrasound in localizing nonpalpable breast lesions over the five-year period in a medical center where intraoperative ultrasound is used routinely. Our aim was to determine the success rate in detecting and adequately removing nonpalpable lesions.

All 155 (100%) preoperatively diagnosed ultrasound-visible nonpalpable lesions in 144 patients (61

do operacije. Jedina ograničenja u primeni ultrazvuka se odnose na edukovanost hirurga i opremljenost hirurške sale ultrazvučnim aparatom, kao i na lezije koje se ne vizualizuju ultrazvukom.

U našem radu analizirali smo upotrebu intraoperativnog ultrazvuka u lokalizovanju nepalpabilnih lezija u dojci u petogodišnjem periodu u medicinskom centru u kome se intraoperativni ultrazvuk rutinski koristi. Naš cilj je bio da utvrdimo procenat uspešnosti nalaženja i adekvatnog uklanjanja nepalpabilnih lezija.

Od 155 preoperativno dijagnostikovanih ultrazvukom vidljivih nepalpabilnih lezija kod 144 pacijentkinje (61 maligna, 94 benigne), koje su operisane pomoću IOUZ lokalizovanja, svih 155 je uspešno identifikovano i hirurški uklonjeno (100%). Ovo je rezultat koji je u skladu sa rezultatima većine publikovanih studija [1-15], gde je procenat uspešnosti lokalizovanja nepalpabilnih lezija intraoperativnim ultrazvukom 100% ili 99%. Ovaj procenat uspešnosti je bolji u odnosu na preoperativno mamografsko lokalizovanje, koje je na osnovu podataka iz literature neuspešno u 2% – 10% slučajeva [3,8].

ZAKLJUČAK

Alternativni modaliteti vizualizacionog lokalizovanja nepalpabilnih lezija u dojci podrazumevaju preoperativno lokalizovanje i obeležavanje mesta lezije plasiranjem obeleživača (žičana igla, radioaktivni obeleživač) ili obeležavanjem mesta projekcije lezije na koži dojke, pod kontrolom ultrazvuka ili mamografije.

Intraoperativno ultrazvučno lokalizovanje nepalpabilnih lezija ima višestruke prednosti nad preoperativnim obeležavanjem: 1) vizualizacija u realnom vremenu, dok traje hirurška procedura; 2) neograničena mogućnost ponavljanja i provere tačnosti lokalizacije nepalpabilne lezije u dojci; 3) nepostojanje rizika migracije markera u vremenu od preoperativnog obeležavanja do izvođenja hirurškog zahvata; 4) nepostojanje rizika nepreciznosti preoperativnog obeležavanja, zbog, na primer, delimično drugačijeg položaja pacijenta tokom preoperativnog obeležavanja u odnosu na položaj pacijenta na operacionom stolu.

Čak i neznatno remećenje pozicije preoperativnog obeležavanja ne može se popraviti nikakvom naknadnom intervencijom na hirurškom stolu, a može voditi neadekvatnoj operaciji, tj. propustu da se iz dojke ukloni nepalpabilna lezija koja je bila cilj operacije.

Ograničenost korišćenja intraoperativnog ultrazvuka u hirurgiji nepalpabilnih lezija u dojci odnosi se na lezije koje se zbog svojih morfoloških karakteristika teško vizualizuju ultrazvukom, pre svega mikrokalcifikati (DCIS). U ovim slučajevima neophodno je preoperativno lokalizovanje takvih lezija mamografom, kao dija-

malignant and 94 benign) who were operated on using intraoperative ultrasound were successfully identified and surgically removed. This result is consistent with the results of most published studies [1-15], where the success rate of localizing nonpalpable lesions using intraoperative ultrasound was 100% or 99%. This success rate is better than in preoperative mammographic localization, which is, according to literature, unsuccessful in 2%-10% of cases [3,8].

CONCLUSION

Alternative modalities of image-guided localization of nonpalpable breast lesions include preoperative localization and marking the site of the lesion by inserting a marker (a wire needle or a radiographic marker), or projection-marking on the skin of the breast under the control of ultrasound or mammography.

Intraoperative ultrasound localization of nonpalpable lesions has multiple advantages over preoperative marking: 1) real-time vizualization, during the surgical procedure; 2) unlimited possibility of repeating and checking the accuracy of the localization of a nonpalpable breast lesion; 3) the absence of the marker-migration risk in the period of time between preoperative marking and the surgical procedure; 4) the absence of the risk of inaccurate preoperative marking due to, for example, a partially different position of the patient during preoperative marking compared to the position of the patient on the operative table.

Even a slight disturbance of the preoperative marking position cannot be corrected by any subsequent intervention on the operative table, and it could lead to inadequate surgery, i.e., a failed attempt to remove the nonpalpable lesion from the breast, which was the initial aim of the surgery.

A limitation in using intraoperative ultrasound in surgical management of nonpalpable breast lesions refers to the lesions that are difficult to visualize with ultrasound due to their morphological characteristics (primarily microcalcifications – DCIS). In these cases, it is necessary to preoperatively localize such lesions using mammography as a diagnostic technique that visualizes such changes well, marking the lesion location with a wire needle.

The optimal quality of nonpalpable breast lesion surgery is achieved by an adequate choice of a localizing technique, whereby intraoperative ultrasound has absolute advantages over preoperative ultrasound localization, except in the case of a lesion that is not ultrasound-visible and is detected by mammography when preoperative marking with the help of mammography should be applied.

Conflict of interest: None declared.

gnostičkom tehnikom koja ove promene dobro vizualizuje, uz obeležavanje lokacije lezija žičanom iglom.

Optimalni kvalitet hirurgije nepalpabilnih lezija u dojci postiže se adekvatnim izborom tehnike lokalizovanja, pri čemu intraoperativni ultrazvuk ima apsolutne prednosti nad preoperativnim ultrazvučnim lokalizovanjem, dok u slučaju ultrazvukom nevidljivih a mamografski detektabilnih lezija treba primeniti preoperativno obeležavanje uz pomoć mamografa.

Sukob interesa: Nije prijavljen.

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