



Biopsja węzłów chłonnych z użyciem ferromagnetyków

Andrzej Kurylcio

Klinika Chirurgii Onkologicznej,
Uniwersytet Medyczny w Lublinie



KONFLIKT INTERESÓW

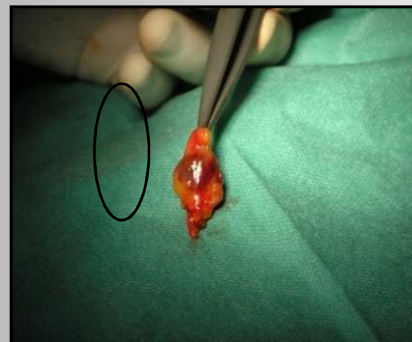


✓ *pokrycie kosztów wyjazdu (travel honorarium)*

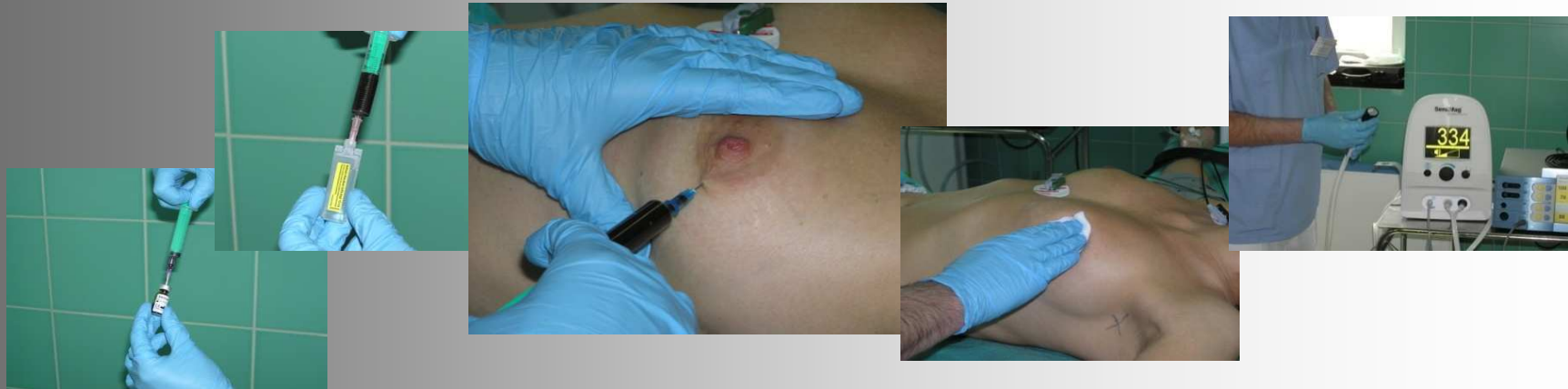
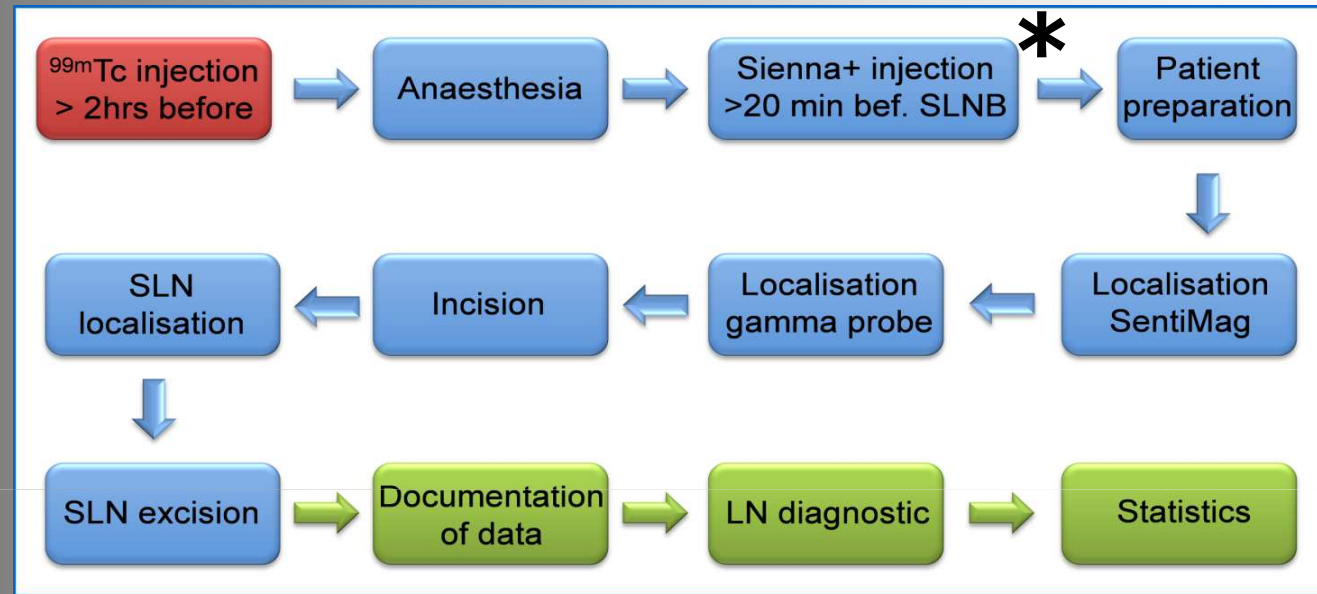
WPROWADZENIE



- ✓ SNB metoda ferromagnetyczna SentiMag®:
 - ✓ nieizotopowa metoda identyfikacji SN:
 - ✓ superparamagnetyczny tlenek żelaza (SPIO; Sienna+®; Magtrace®)
 - ✓ czarno-brązowa wodna jałowa zawiesina
 - ✓ podanie podskórne śródmiąższowe podotoczkowo, okołoguzowe
 - ✓ ręczny magnetometr (SentiMag®)
 - ✓ śródoperacyjna identyfikacja SN: magnetometr + kolor



MATERIAŁ I METODYKA



* od maja 2016 r. podanie Sienna+ ok.18 - 24 godz. przed SNB

MATERIAŁ I METODYKA



METODA ("non-inferiority studies")



Douek M, Klasse J, Monypenny I, et al. Sentinel node biopsy using a magnetic tracer versus standard technique: the SentiMAG Multicentre Trial. Ann Surg Oncol 2014

Thill M, Kurylcio A, Welter R, et al. The Central-European SentiMag Study: sentinel lymph node biopsy with superparamagnetic iron oxide (SPIO) versus radioisotope. Breast 2014

Rubio IT, Diaz-Botero S, Esgueva A et al. The super paramagnetic iron oxide is equivalent to the Tc99 radiotracer method for identifying the sentinel node in breast cancer. EJSO 2015

Pinero-Madrone A, Torro-Richart JA, de Leon-Carrillo JM et al. Superparamagnetic iron oxide as a tracer for sentinel node biopsy in breast cancer: A comprehensive non-inferiority study – The Imagine Study. EJSO 2015

Houpeau JL, Chauvet MP, Guillemin F. et al. Sentinel lymph node identification using superparamagnetic iron oxide particles versus radioisotope: The French Sentimag feasibility trial. J Surg Oncol. 2016

Karakatsanis A, Christiansen PM, Fischer L et al. The Nordic SentiMag trial: a comparison of super paramagnetic iron oxide (SPIO) nanoparticles versus Tc99 and patent blue in the detection of sentinel node (SN) in patients with breast cancer and meta-analysis of earlier studies, Breast Cancer Res Treat 2016

współczynnik identyfikacji: 94,4% - 98%

DYSKUSJA

Ferrucci M, Franceschini G, Douek M New techniques for sentinel node biopsy in breast cancer . Transl Cancer Res 2018

Advantages

- ✓ real time visualization
- ✓ cheap
- ✓ quick
- ✓ no nuclear medicine department needed
- ✓ no severe allergic reactions reported



Disadvantages

- ✓ low molecular weight
- ✓ ICG leaking out after SLN is recised
- ✓ difficult to be detected at a depth of more than 1 cm
- ✓ can not be used in patients with iodine allergy

Advantages

- ✓ short preparation time
- ✓ comfortable timeframe
- ✓ appropriate molecular weight
- ✓ several years shelf-life
- ✓ fast learning curve
- ✓ brown colour helps during axillary dissection
- ✓ do not require any special storage
- ✓ no nuclear medicine department needed
- ✓ no severe allergic reactions reported



Disadvantages

- ✓ large diameter of the magnetomer
- ✓ regular re-balancing of the probe during usage
- ✓ possible interference of the surgical instrumentation with the ferromagnetic signalling
- ✓ magnetometer does not reach the same depth as a gamma probe
- ✓ intra-mammary persistence which can create void MRI artefacts
- ✓ can not be used in patients with hypersensitivity to iron or dextran compounds and those with pacemakers or metal implants

DYSKUSJA (CTH)



Rubio IT., Diaz – Botero S., Esgueva AJ, et al. Increased detection of sentinel nodes in breast cancer patients with the use of spio tracer.

Journal of Clinical Oncology suppl 2014

- ✓ detection rate 100%

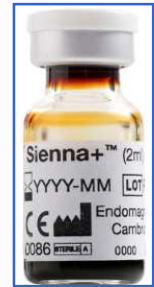
Qiu SQ, Zang GJ, Jansen L. al. Evolution in sentinel lymph node biopsy in breast cancer *Critical Reviews in Oncology /Hematology 2018 :*

- ✓ new techniques for SNB:
 - ✓ Indocyaninengreen optical imaging guided SNB
 - ✓ Superparamagnetic iron oxide guided SNB
 - ✓ Higher SN retrieval number and lower FNR
 - ✓ **Potentially optimal tracer for SNB after NAC**



Ersoy YE, Kadioglu H. Review of Novel Sentinel Lymph Node Biopsy Techniques in Breast Cancer Patients Treated with Neoadjuvant Chemotherapy. *Clinical Breast Cancer 2018*

DYSKUSJA



Bazire L, Alran S, Bamrani S El et al. Radiation therapy after sentinel node biopsy for early stage breast cancer using a magnetic tracer: Results of a single institutional prospective study of tolerance. *Cancer/ Radiotherapie* 2019

- ✓ 288 pts: 87,5% BCT 50 Gy, 25 frakcji + boost
- ✓ IR 99,7%
- ✓ 95.8% radiodermatitis 0-2 grade / 19.4% posttherapeutic fibrosis 1 – 2 grade

No increase of the toxicity was observed

Karakatsanis A, Daskalakis K, Stalberg P et al. Superparamagnetic iron oxide nanoparticles as the **sole method** for sentinel node biopsy detection in patients with breast cancer. *BJS* 2017.

- ✓ Spio injection preoperative (1-4 weeks before surgery) or perioperative (1 hour)
- ✓ DR 95,6%
- ✓ Preop SPIO injection resulted in harvesting of more SN: 1,43 vs 1,03
- ✓ Less staining in pts with deeper peritunoral injection
- ✓ Cost analysis: 225 euro SPIO vs 252 euro Tc99
 - ✓ Preop vs periop injection:
 - ✓ 17,6 euro per min for the operating theatre
 - ✓ 352,7 euro seved per procedure



Effective method , safe alternative

DYSKUSJA



Warnberg F, Stigberg E, Obondo Ch et al. Long term outcome **after retro-aerolar versus peri-tumoral** injection of superparamagnetic ironoxide nanoparticles (SPIO) for sentinel lymph node detection in breast cancer surgery. *Ann Surg Oncol* 2019

- ✓ Retro-aerolar vs close to palpable tumors or in the peritumoral area for nonpalpable SPIO injection
- ✓ Skin staining: 67,3% retro-aerolar, 37,8% peritumoral (diminished over time - 46 vs 9,4 after 36 months)
- ✓ IR: 97,9%: 98,3% retro-aerolar/97,4% peritumoral
- ✓ 98,0% 1-27 days before/94,25% on the day
- ✓ Mean number of removed SN: 1,35 retroaerolar/1,57 peritumoral injection
- ✓ 1,56 1 to 27 days/1,27 – mean number of SN significantly higher
- ✓ Pts with lower BMI – higher detection rate (100% vs 93,3%); similar number of SN
- ✓ M or BCS - similar detection rate 98,7%/97,5%; mean number of SN 1,29 vs 1,51
- ✓ Less/smaller skin staining after peritumoral injection; comparable DR
- ✓ Injection of SPIO before the day of surgery increased SN detectio rate by 4%

DYSKUSJA



Warnberg F, Stigberg E, Obondo Ch et al. Long term outcome **after retro-aerolar versus peri-tumoral** injection of superparamagnetic ironoxide nanoparticles (SPIO) for sentinel lymph node detection in breast cancer surgery. *Ann Surg Oncol* 2019

- ✓ Possibility to inject SPIO up to 4 weeks before surgery – flexibility, easy logistics
- ✓ reduce staining artefacts in post-op MRI: updated SPIO – in volume of 1,5 and 1ml without dilution (?)
- ✓ Magnetic clip + spio – injection at outpatient clinic 4 weeks before surgery – logistic benefits
- ✓ Preoperative diagnosis of DCIS – SPIO injection at the time of surgery – SN removing at a second procedure if invasive cancer detected on histopathology
 - ✓ Reduces unnecessary SNB
 - ✓ Saving money
 - ✓ Concept can be applied to prophylactic mastectomy



DYSKUSJA (Magtrace)



Man V, Wong TT Co M et al. Sentinel Lymph Node Biopsy in Early Breast Cancer: Magnetic Tracer as the Only Localizing Agent. World J Surg 2019

- ✓ Larger cohort on use of SPIO in Asian population
- ✓ Subareolar injection of 2 ml - SiennaXP® - **Magtrace®**
- ✓ 99.3% BCS, 98.5% M; median of 4 SNs
- ✓ No allergic reaction
- ✓ Use of SPIO alone saves 22 300 \$ per year compared to dual tracers

Alvarado MD, Mittendorf EA, Teshome M et al. SentimaglC: Non-inferiority Trial Comparing Superparamagnetic Iron Oxide versus Technetium99 and Blue Dye in the Detection of Axillary Sentinel Nodes in Patients with Early Stage Breast Cancer. Ann Surg Oncol 2019

- ✓ **Magtrace** injection 2ml in subareolar region at least 20 min before
- ✓ DR 99,3% vs 98,6%
- ✓ AEs – discoloration 16,3% - deeper injection
- ✓ 100% concordance rate for positive SNs

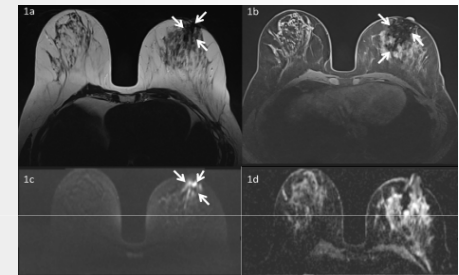
non-inferior to the standard technique

DYSKUSJA (MRI)



Krischer B, Forte S, Niemann T et al. Feasibility of breast MRI after sentinel procedure for breast cancer with superparamagnetic tracers. EJSO 2018

- ✓ 34 pts (25 cases evaluated) who received Sienna® for SNB; mean time since injection 42 months;
- ✓ Follow up MRI; 1,5T model without application of i.v. contrast
- ✓ Residues of SPIO detected in 13 cases (52%)
- ✓ 10 cases (40%) MR imaging quality impaired
- ✓ 3 cases (12%) MRI impossible to interpret
- ✓ 12 cases (48%) showed no restriction
- ✓ No tracer residues found in the axilla



Karakatsanis A, Obondo Ch, Abdsaleh S et al. Optimisation of breast MRI compatibility after sentinel node biopsy with paramagnetic tracers. EJSO 2018 (correspondence)

- ✓ Unpublished data - SPIO artefacts seen in postop MRI of pts with discoloration
- ✓ Excision of injected tissue / deeper peritumoral injection
- ✓ Volume of SPIO injected (2+3 ml)
- ✓ Ongoing multicentre study SentiDose <https://doi.org/10.1186/ISRCTN11156955>)
SiennaXP reduces dose 1.5 and 1 ml for SN
- ✓ prospective multicentre trial "POSToperative breast MRI in pts undergoing SNB using super paraMAGnetic iron oxide nanoparticles" (POSTMAG MRI, <https://doi.org/10.1186/ISRCTN85167182>)

DYSKUSJA (Magseed)



Ahmed M, Anninga B, Goyal S et al. Magnetic sentinel node and occult lesion localization in breast cancer (MagSNOLL Trial) BJS 2015

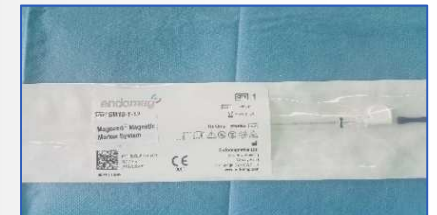
- ✓ Magnetic localization is feasible with intratumoral magnetic tracer injection

Price E, Khoury A, Esserman L et al. Initial Clinical Experience with an Inducible Magnetic Seed System for Preoperative Breast Lesion Localization. AJR 2018

- ✓ Evaluation of magnetic seed system: 73 seeds placed and retrieved intraop. successfully
- ✓ Magseed 5x1 mm; 18-gauge preloaded needle; under MMG or USG up to 30 days
- ✓ Effective alternative to wire placement

Pohlodek K, Foltin M, Meciarova I et al. Simultaneous use of magnetic method in localization of impalpable breast cancer and sentinel lymph nodes detection: initial Experience. Nanomedicine 2018

- ✓ All impalpable lesions detected and localized
- ✓ All tumors removed with safe margins
- ✓ Mean nodal detection rate 3.4
- ✓ No interferences between signals from Magseed/Sienna observed



DYSKUSJA



Lorek A, Stojcev Z, Zarębski W et al. Analysis of postoperative complications after 303 sentinel lymph node identification procedures using the SentiMag method in breast cancer patients. Med Sci Monit 2019

- ✓ IR 99% 303 pts
- ✓ Paresthesias 12 (9,9%) Lymphodema 9 (7,5%) – most pts after M+SNB
- ✓ rate of complications increased with number of dissected LN
- ✓ Discolorations 47 (15,5%) – diminished after 18 months

safe SN identification and low risk of complications

Polska – 23 ośrodki



DOŚWIADCZENIA WŁASNE

technika ferromagnetyczna



- ✓ metoda stosunkowo łatwa do wprowadzenia do praktyki
 - ALE: doświadczony w SNB chirurg*
- ✓ prosta w codziennym stosowaniu
- ✓ podobny czas preparatyki SN
- ✓ konieczność używania plastikowych narzędzi
- ✓ trudniejsza preparatyka u otyłych chorych
- ✓ niezależnienie od pracowni medycyny nuklearnej
- ✓ łatwa identyfikacja 2 – 4 SN (zalecenia PTChO, St. Gallen, NCCN) u chorych poddanych NACTH, wycięciom diagnostycznym
- ✓ potencjalna możliwość artefaktów w MRI
- ✓ koszty ! (sprzęt, znacznik, narzędzia)
- ✓ rozwój technik ferromagnetycznych –



MAGSEED



WNIOSKI doświadczenia własne



Sześćcioletni okres doświadczeń pozwala na stwierdzenie,
że **SNB metodą ferromagnetyczną**
jest efektywną i bezpieczną metodą lokalizacji.

W rękach doświadczonego chirurga pozwala osiągnąć **wysoki
odsetek identyfikacji**, średnio 3 SN,
co zmniejsza odsetek wyników fałszywie ujemnych.