Biopsy: How it is done? Quality/mistakes, prognosis/center

11th SPAEN Annual Conference for Organizations
Representing Patients with Sarcomas, GIST and Desmoids
22-24 April 2021 – Virtual Meeting

Sarcoma Patients EuroNet

Piotr Rutkowski

piotr.rutkowski@pib-nio.pl

Maria Sklodowska-Curie
National Research Institute of Oncology

Narodowy Instytut Onkologii
im. Marii Skłodowskiej-Curie
Państwowy Instytut Badawczy

ESMO-EURACAN guidelines

MULTIDISCIPLINARY APPROACH AND REFERRAL TO SPECIALIST CENTRES IS KEY

Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up

P. G. Casali, N. Abecassis, H. T. Aro, S. Bauer, R. Biagini, S. Bielack, S. Bonvalot, I. Boukovinas, J. V. M. G. Bovee, T. Brodowicz, J. M. Broto, A. Buonadonna, E. De Álava, A. P. Dei Tos, X. G. Del Muro, P. Dileo, M. Eriksson, A. Fedenko, V. Ferraresi, A. Ferrari, S. Ferrari, A. M. Frezza, S. Gasperoni, H. Gelderblom, T. Gil, G. Grignani, A. Gronchi, R. L. Haas, B. Hassan, P. Hohenberger, R. Issels, H. Joensuu, R. L. Jones, I. Judson, P. Jutte, S. Kaal, B. Kasper, K. Kopeckova, D. A. Krákorová, A. Le Cesne, I. Lugowska, O. Merimsky, M. Montemurro, M. A. Pantaleo, R. Piana, P. Picci, S. Piperno-Neumann, A. L. Pousa, P. Reichardt, M. H. Robinson, P. Rutkowski, A. A. Safwat, P. Schöffski, S. Sleijfer, S. Stacchiotti, K. Sundby Hall, M. Unk, F. Van Coevorden, W.T.A. van der Graaf, J. Whelan, E. Wardelmann, O. Zaikova & J. Y. Blay, on behalf of the ESMO Guidelines Committee and EURACAN

STSs are ubiquitous in their site of origin and are often managed with multimodality treatment. A multidisciplinary approach is, therefore, mandatory in all cases, involving pathologists, radiologists, surgeons, radiation therapists, medical oncologists and paediatric oncologists, as well as nuclear medicine specialists and organ-based specialists, as applicable. Management should be carried out in reference centres for sarcomas and/or within reference networks sharing multidisciplinary expertise and treating a high number of patients annually. These centres are involved in ongoing clinical trials, in which the enrolment of sarcoma patients is common. This centralised referral should be pursued as early as at the time of the clinical diagnosis of a suspected sarcoma. In practice, referral of all patients with a lesion likely to be a sarcoma would be recommended. This would mean referring all patients with an unexplained deep mass of soft tissues, or with a superficial lesion of soft tissues having a diameter of >5 cm. Quality criteria are needed for sarcoma reference centres and, increasingly, reference networks.

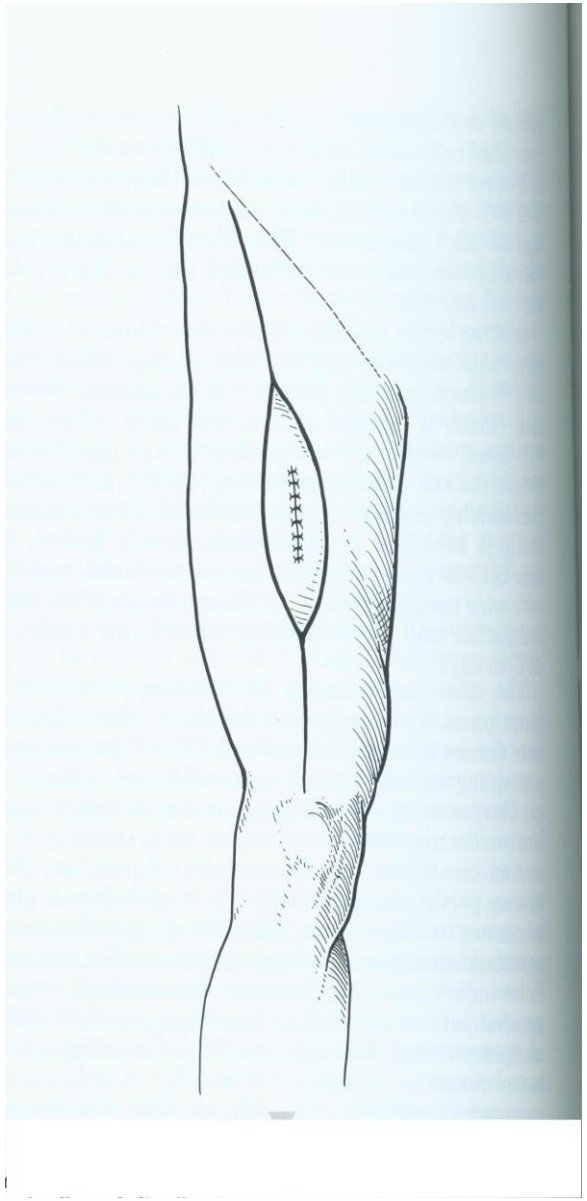
Refer the following tumours to a reference centre for biopsy, diagnosis and treatment:

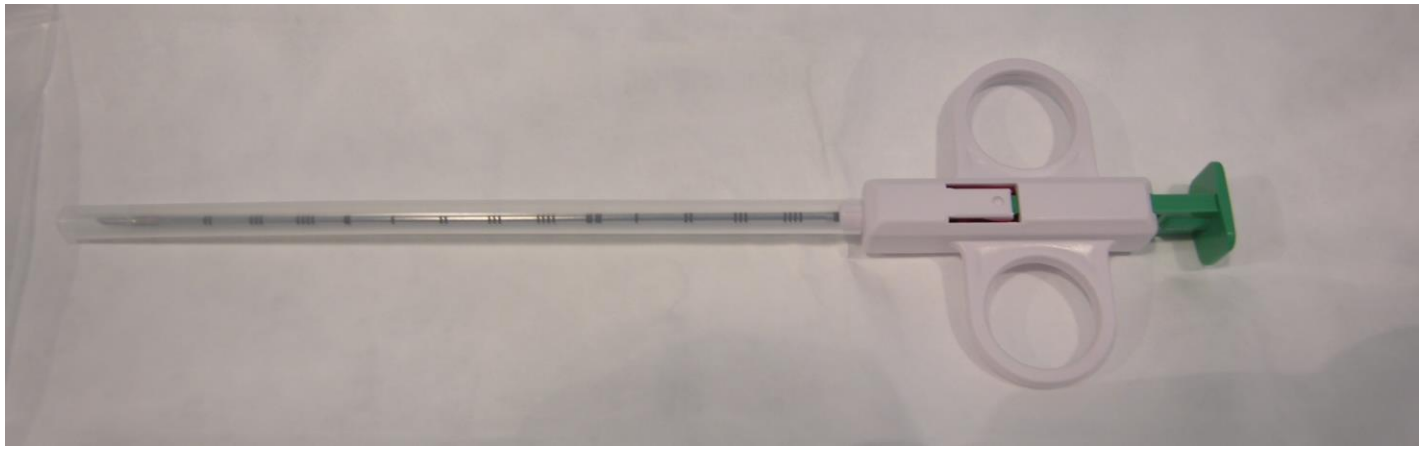
Superficial tumours > 5 cm in diameter

All deeply located tumours (below the muscle fascia)

ESMO-EURACAN, European Society for Medical Oncology-European Reference Network for rare adult solid cancers; STSs, soft tissue sarcomas

Cascali, PG et al. Ann Oncology 2018;29:iv51-iv67.





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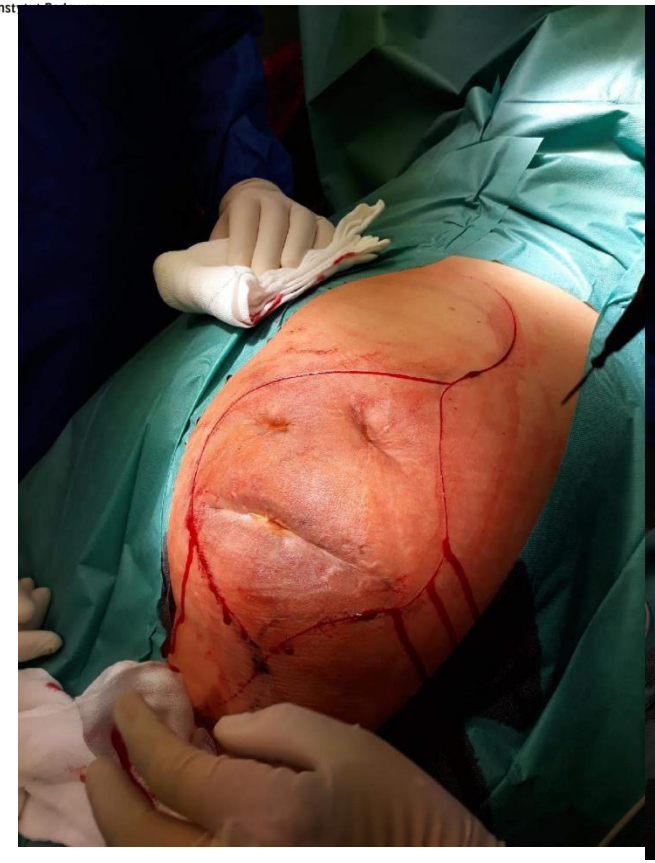
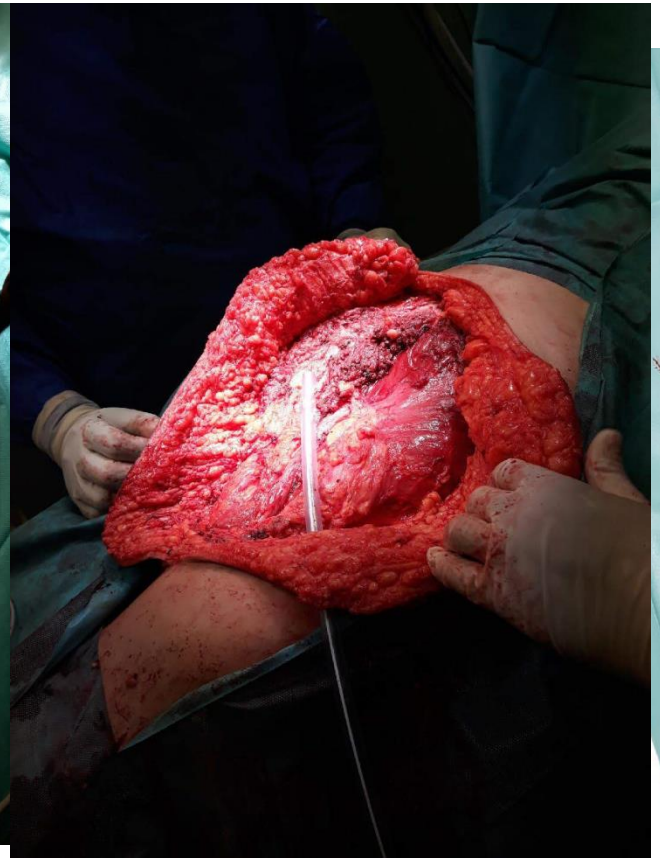
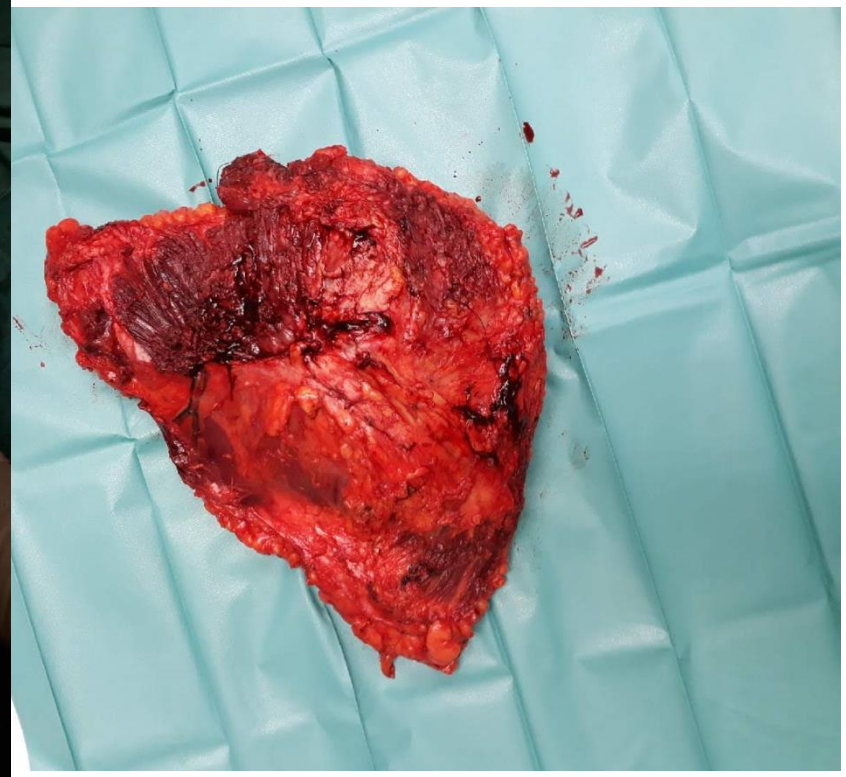


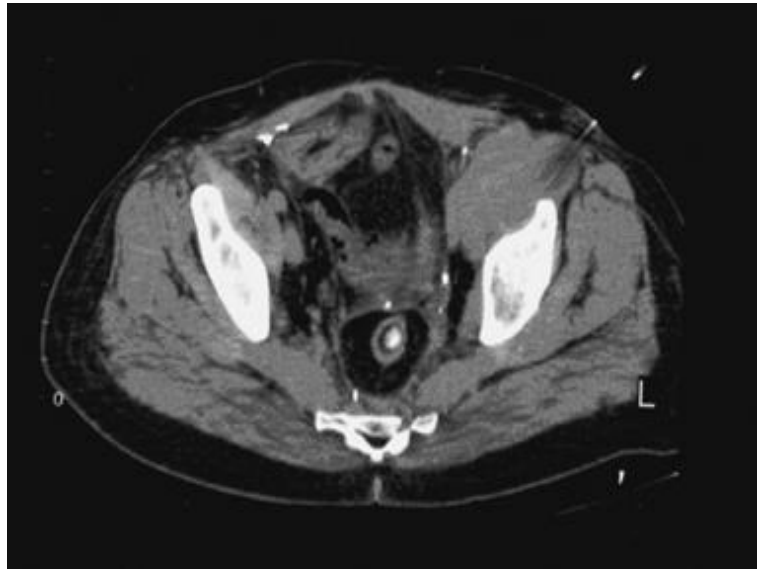


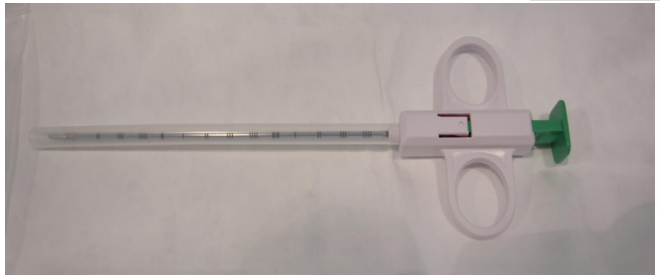


Importance of diagnostic biopsy in soft tissue sarcoma

SARCOMA – CORE NEEDLE BIOPSY
NOT OFTEN PERFORMED!

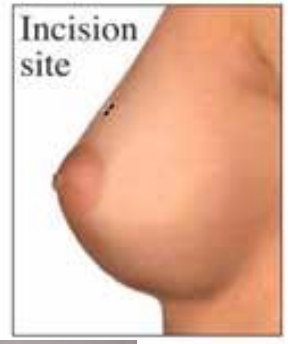
90 mm!

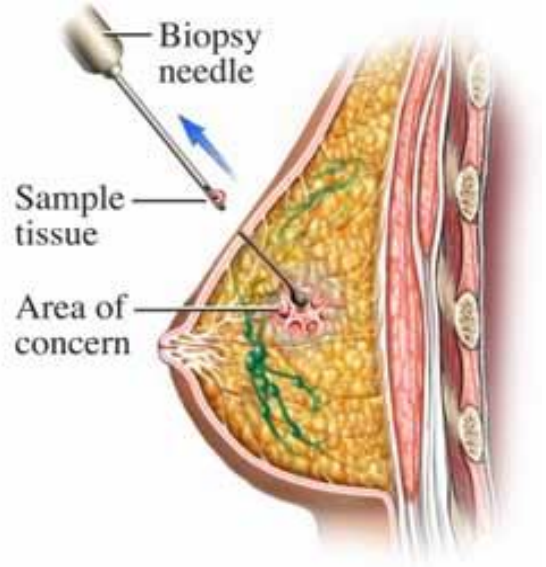




BREAST TUMOUR – CORE NEEDLE BIOPSY
ALWAYS PERFORMED!

7 mm!





Patient scans provided by Rutkowski P, personal communication 2019

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Accuracy of Biopsy Techniques for Limb and Limb Girdle Soft Tissue Tumors

Ina Hoeber, Andrew J. Spillane, FRACS, Cyril Fisher MA, MD, FRCPath,
and J. Meirion Thomas MS, MRCP, FRCS

TABLE 4. *Accuracy of Tru-cut biopsy in the diagnosis of STS from benign STT and subtype of STT*

	Final histology STS	Final histology STT (Benign)	
Tru-cut result			
Malignant	179	1	PPV 99.4%
Benign	1	78	NPV 98.7%
	Sensitivity 99.4%	Specificity 98.7%	
Tru-cut subtype result*			
	Correct (%)	Incorrect (%)	Indeterminable (%)
STS n = 179	143 (79.9)	11 (6.1)	25 (14.0)
STT (benign) n = 78	63 (80.8)	6 (7.7)	9 (11.5)
Tru-cut grade result			
	Correct (%)	Incorrect (lower in all cases) (%)	Indeterminable (%)
STS n = 179	152 (84.9)	12 (6.7)	15 (8.4)

* 2 core-needle biopsies excluded because wrong diagnosis given.
PPV, positive predictive value; NPV, negative predictive value.

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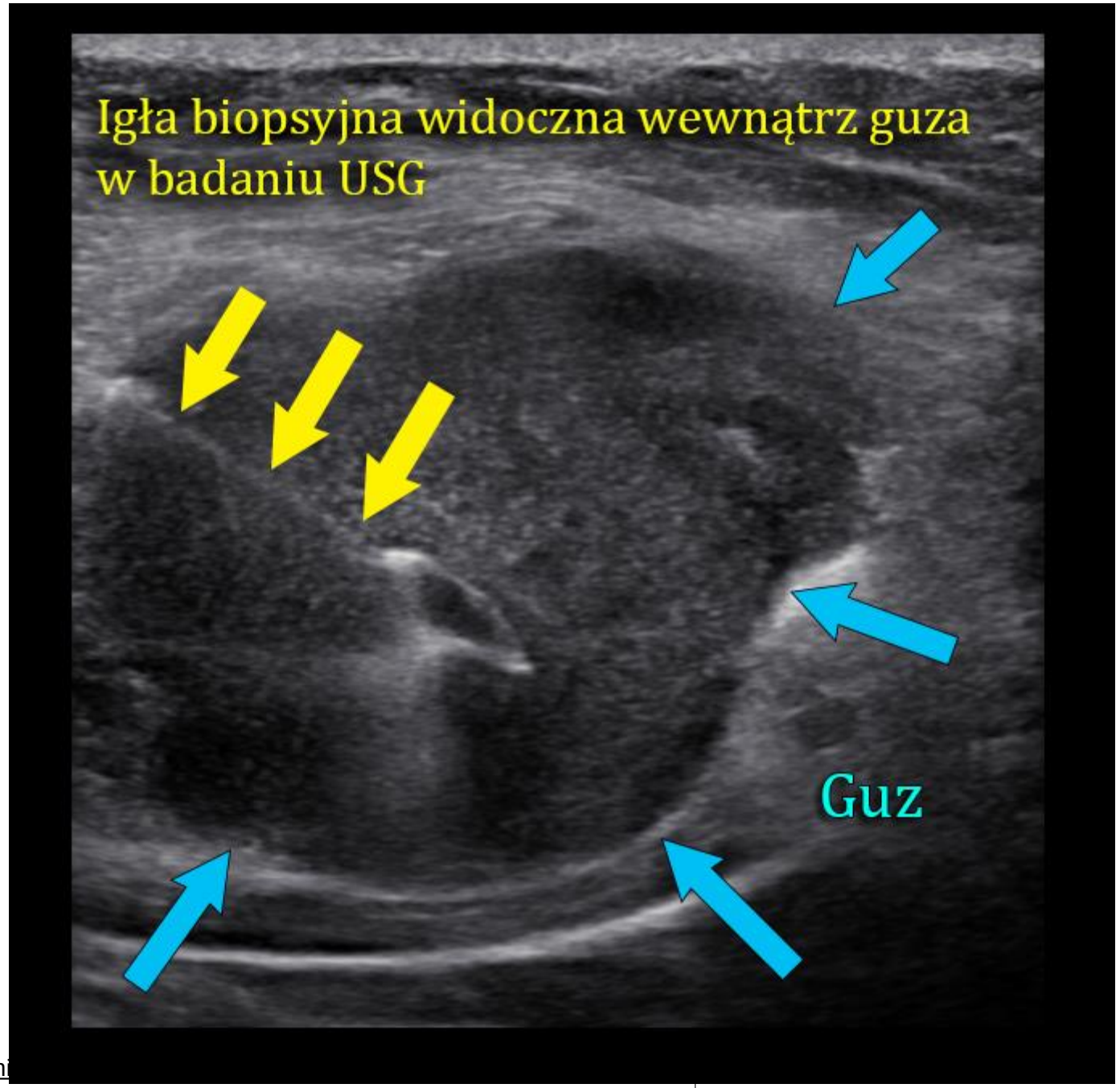

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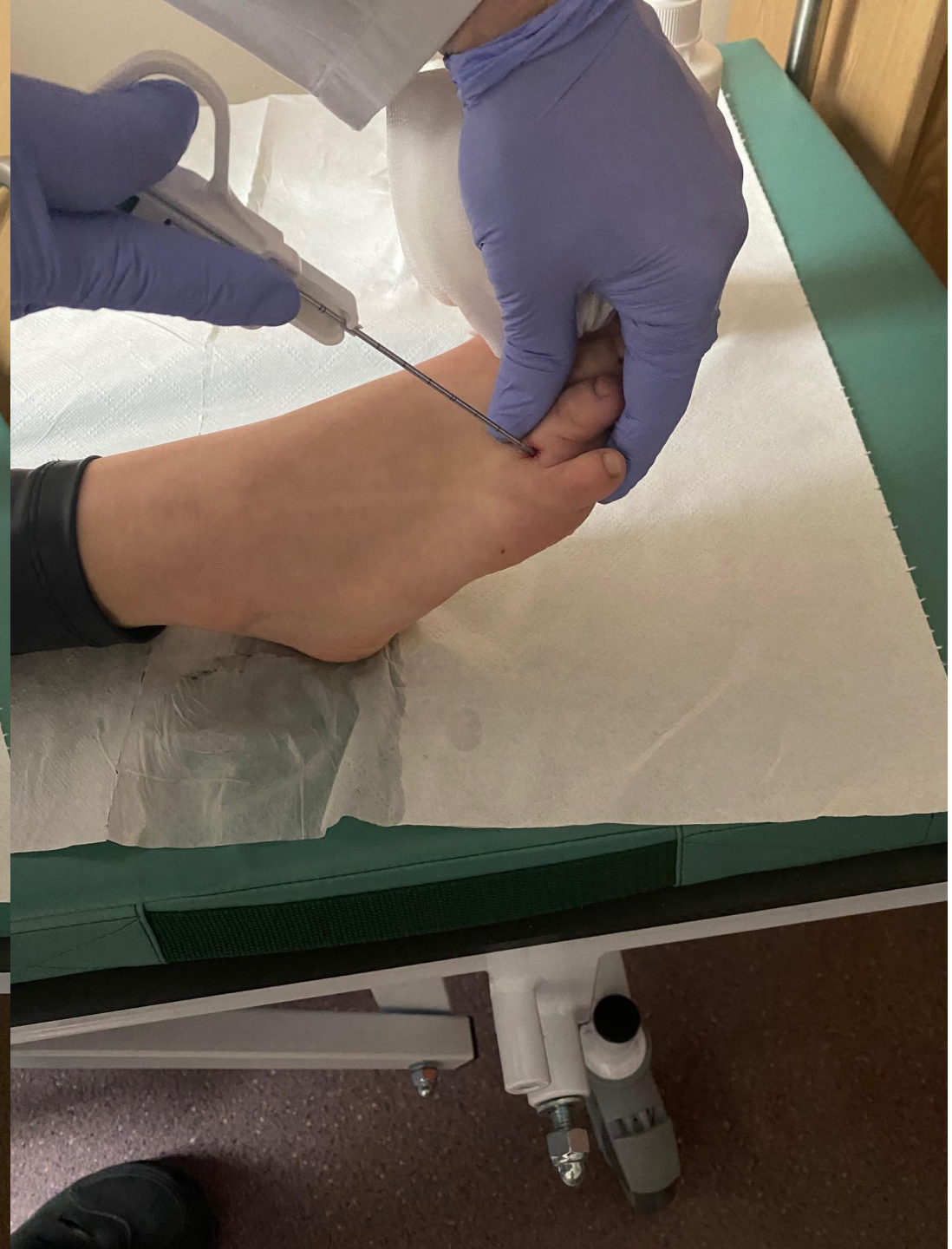

26.04.2021

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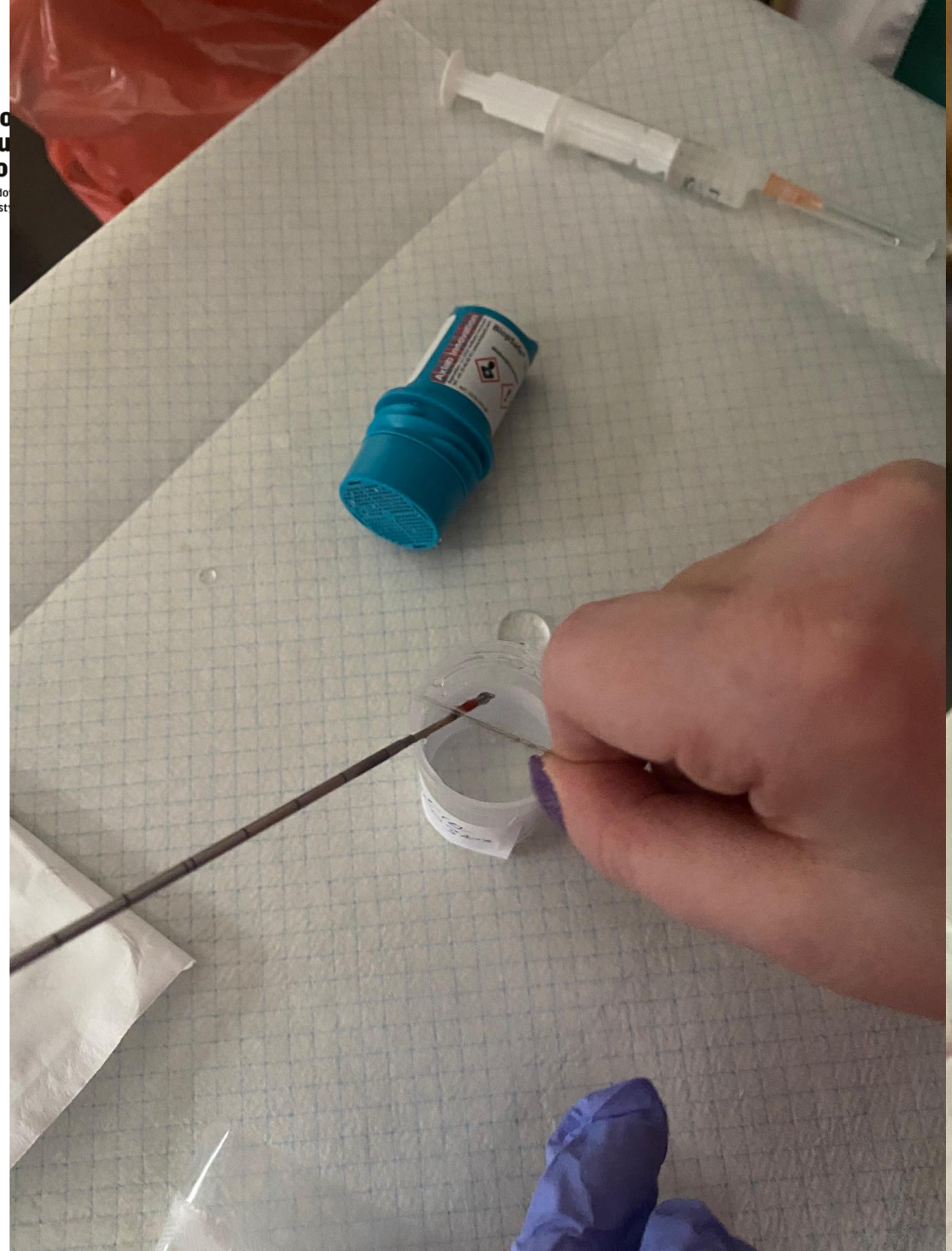

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Original Article

Image-guided core needle biopsy for musculoskeletal lesion

Journal of Orthopaedic Science

Shunichi Toki [a, e, *], Miyuki Sone [b], Akihiko Yoshida [c, d], Toshihiko Nishisho [e], Tabu Gokita [f], Eisuke Kobayashi [a, d], Fumihiko Nakatani [a, d], Hirokazu Chuman [a], Shunsuke Sugawara [b], Yasuaki Arai [b], Akira Kawai [a, d]

Results: Among the 284 studied biopsies, 252 (88.7%) were considered clinically "effective". The sensitivity for detection of malignancy was 94.0% (110/117) and the specificity was 95.3% (41/43). The diagnostic accuracy for detection of malignancy was 94.4% (151/160) and that for histological subtype was 92.3% (48/52). The clinical effectiveness of the procedure was correlated with the complexity of the biopsy route ($P = 0.015$); the trans-pedicular, trans-retroperitoneal and trans-sciatic foramen approaches tended to yield ineffective results. Repeat biopsy did not have a significant impact on the effectiveness of image-guided CNB ($P = 0.536$).

Conclusions: The diagnostic accuracy rates of image-guided CNB performed at multidisciplinary sarcoma units were usable even for patients who have variety of diagnostic biopsy procedures. It is important to establish and implement diagnostic strategies based on an understanding that complicated routes, especially for spine and pelvic lesions, may be associated with ineffectiveness and/or complications.

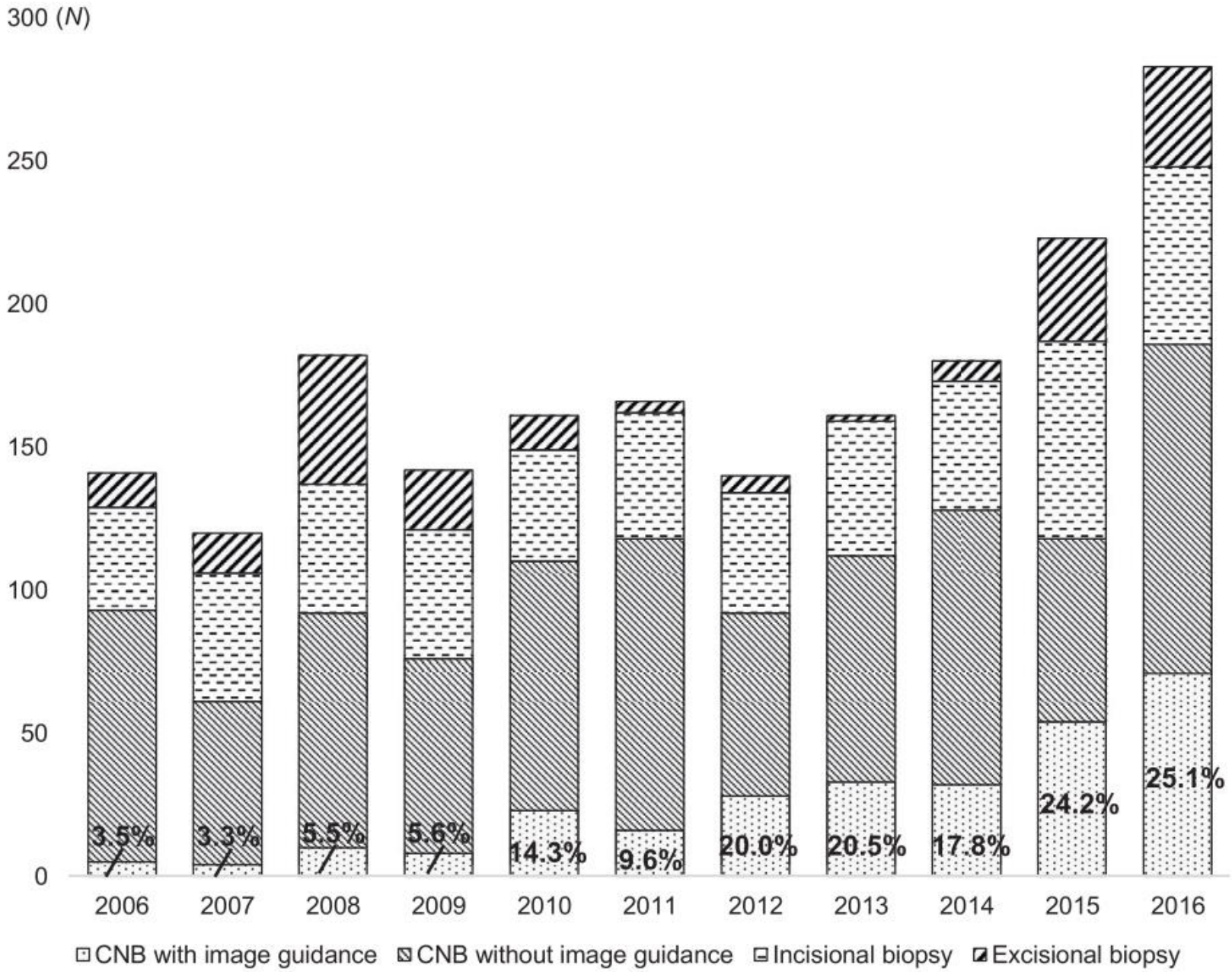

Fig. 1. Changes in the number and distribution of biopsy procedures for musculoskeletal lesions at our institution from 2006 to 2016. CNB, core needle biopsy.

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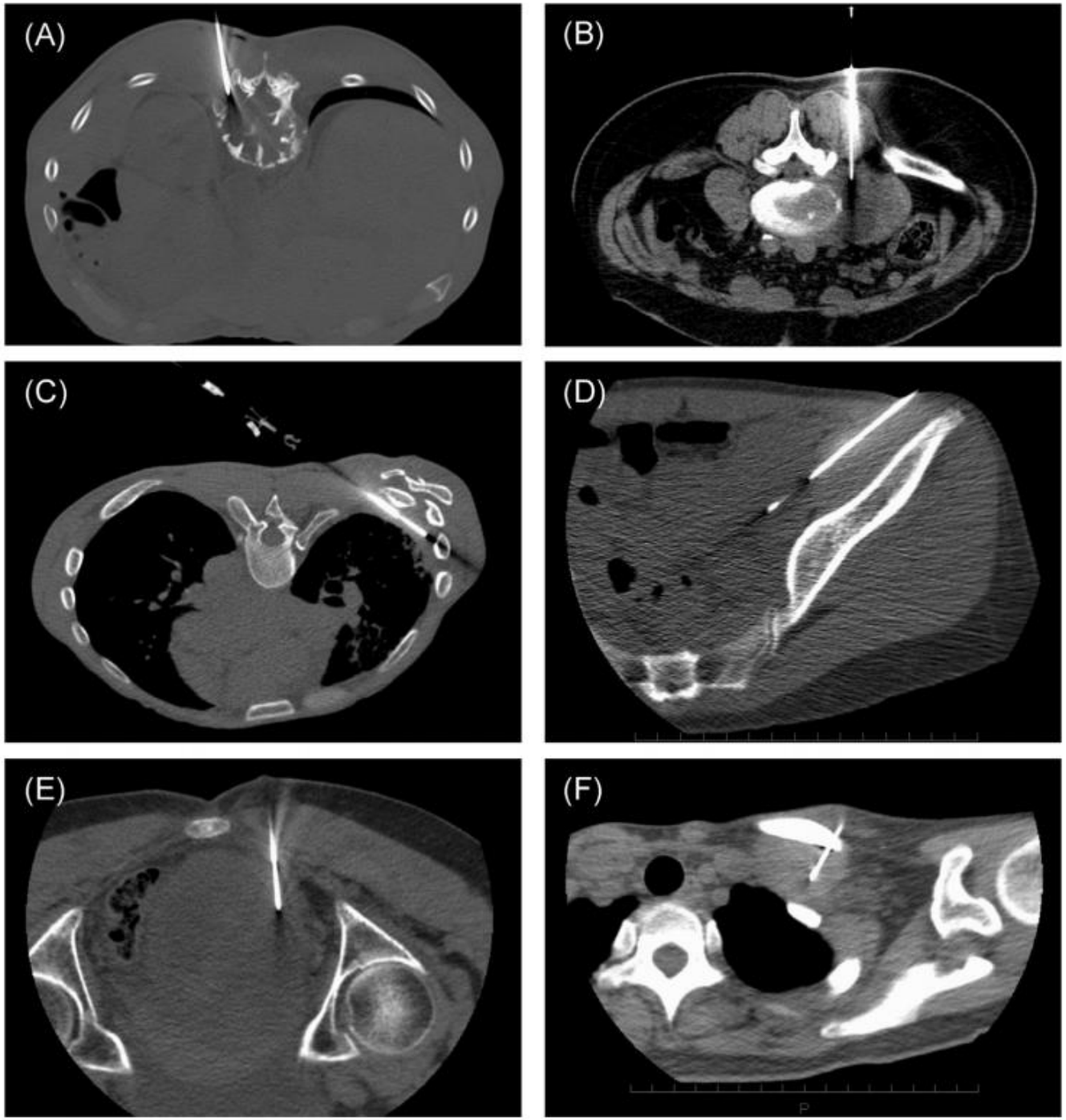
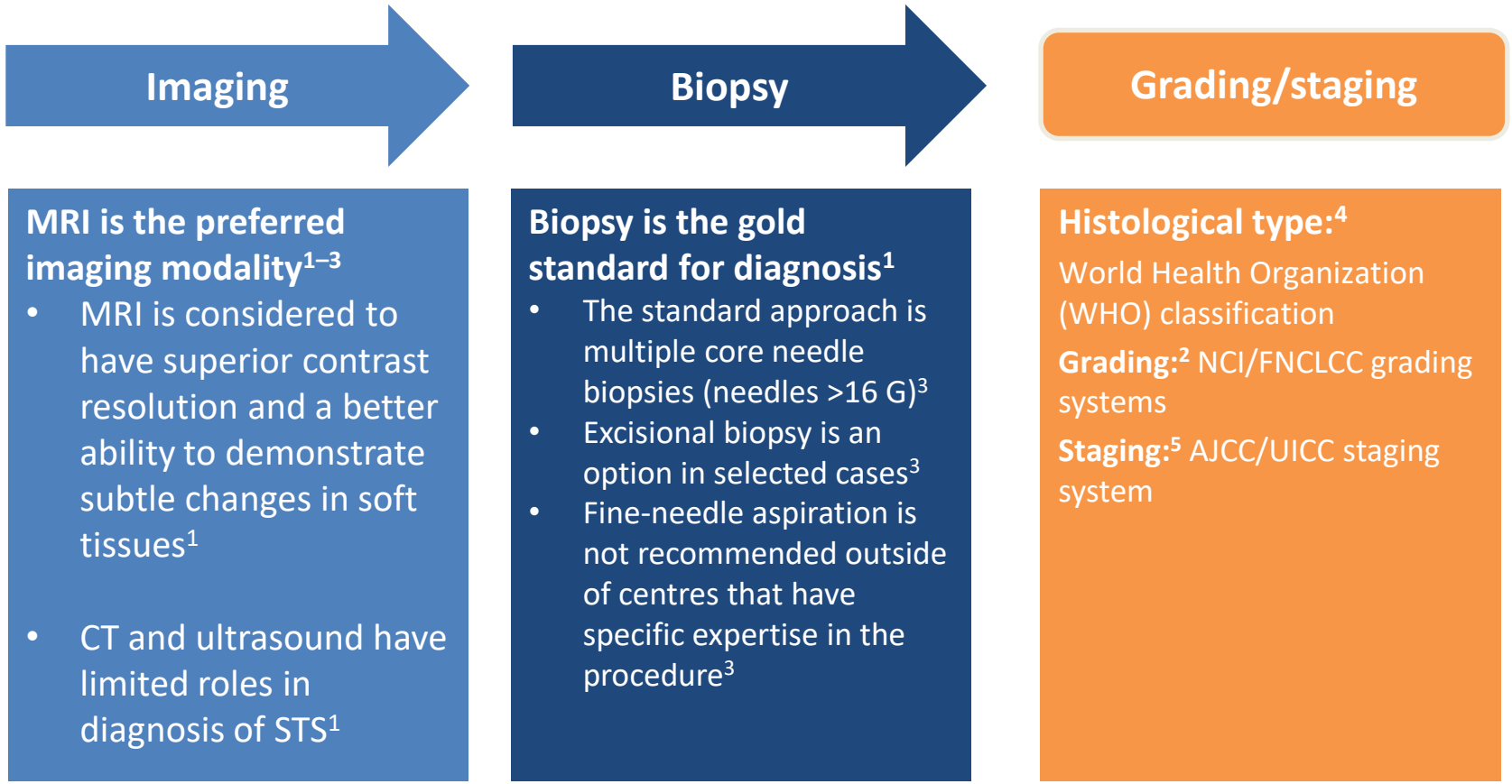


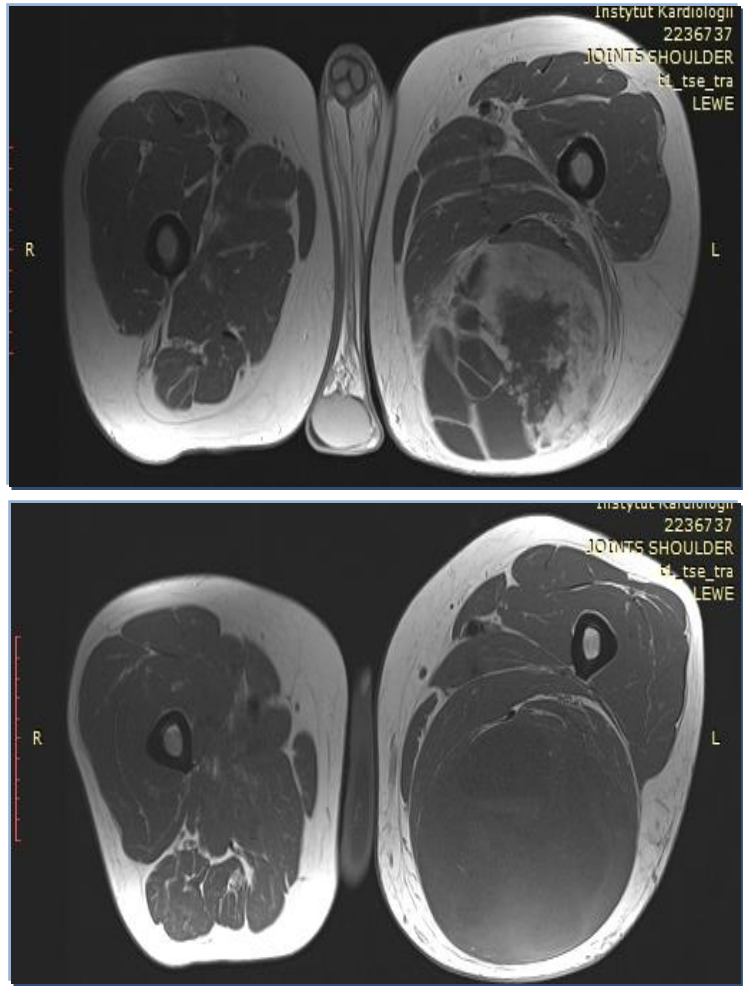
Standard diagnostic procedures

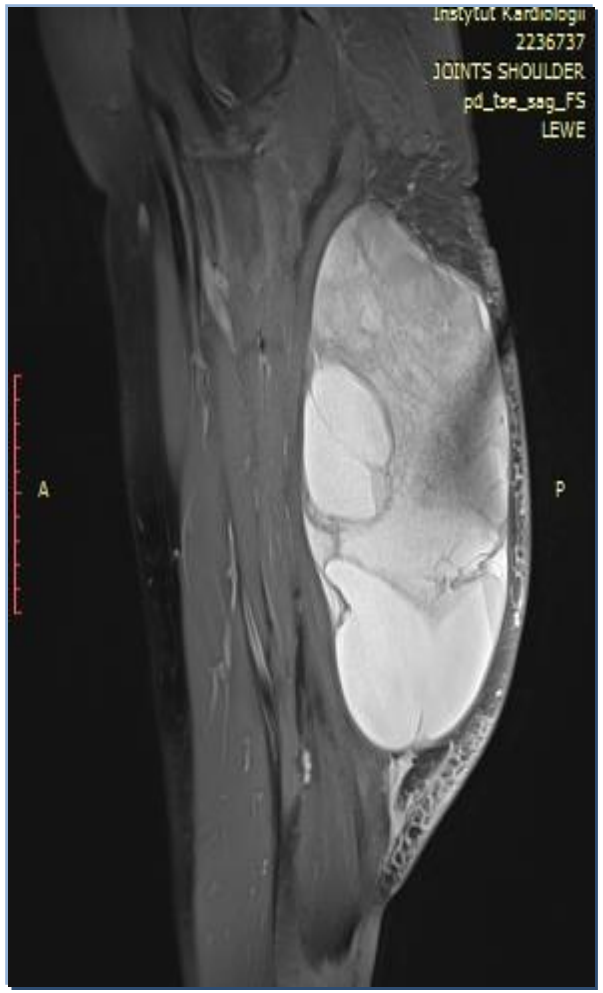


AJCC, American Joint Committee on Cancer; CT, computed tomography; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer; MRI, magnetic resonance imaging; NCI, National Cancer Institute; STS, soft tissue sarcoma; UICC, International Union Against Cancer; WHO, world health organisation

1. Ilaslan H, et al. Cleve Clin J Med 2010;77 Suppl 1:S2; 2. Grimer R, et al. Sarcoma 2010;2010:506182;
3. Casali P & Blay JY. Ann Oncol 2010;21:198; 4. Fletcher C, et al. Pathology and Genetics of Tumours of Soft Tissue and Bone. World Health Organization Classification of Tumours. 2012; 5. Edge S, et al. AJCC Cancer Staging Manual. 7th edn. 2009.

MRI images of STS with internal Heterogeneity





STS, soft tissue sarcoma

Patient scans provided by Rutkowski P, personal communication 2019

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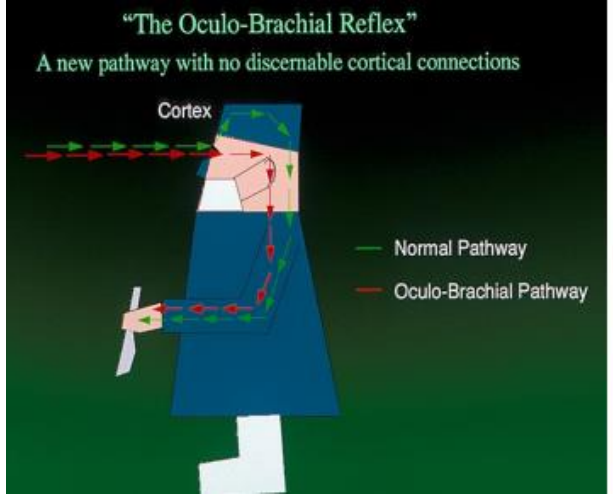
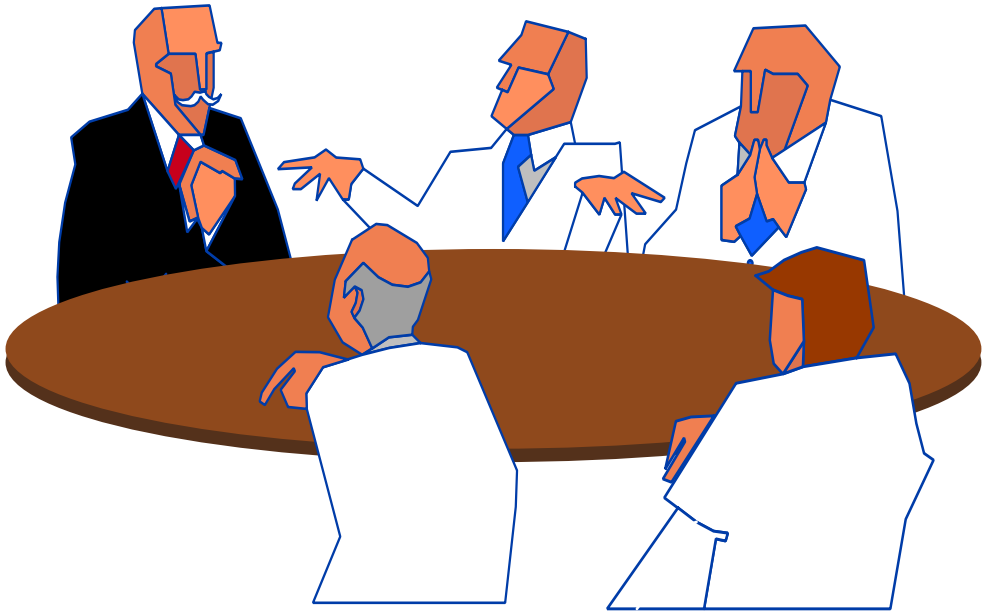


1. Diagnosis?
2. Should it be taken out?
3. Should I be taking it out?
4. What will it involve taking it out?
5. Is it possible/beneficial/risks to resect?



SARCOMA – Current situation – lack of MTD in majority of cases. Does surgeon and perioperative therapy make a difference?

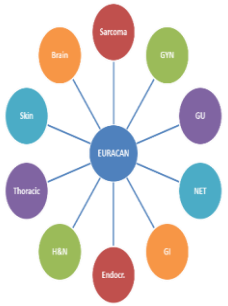
Ist step: I do not know what it is

2nd step: I will operate you immediately!

3rd step: O my God, it was SARCOMA!

4th step: I did my best, now you have to go to Oncologist

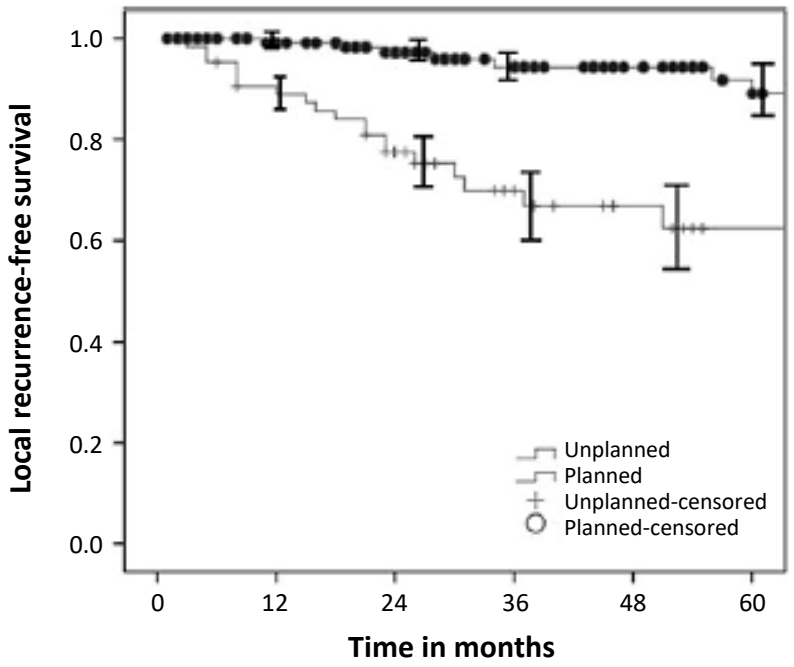
"Nurse, get on the internet, go to SURGERY.COM, scroll down and click on the 'Are you totally lost?' icon."



EURACAN

European network for Rare adult solid Cancer

Unplanned excision of high-grade soft tissue sarcomas



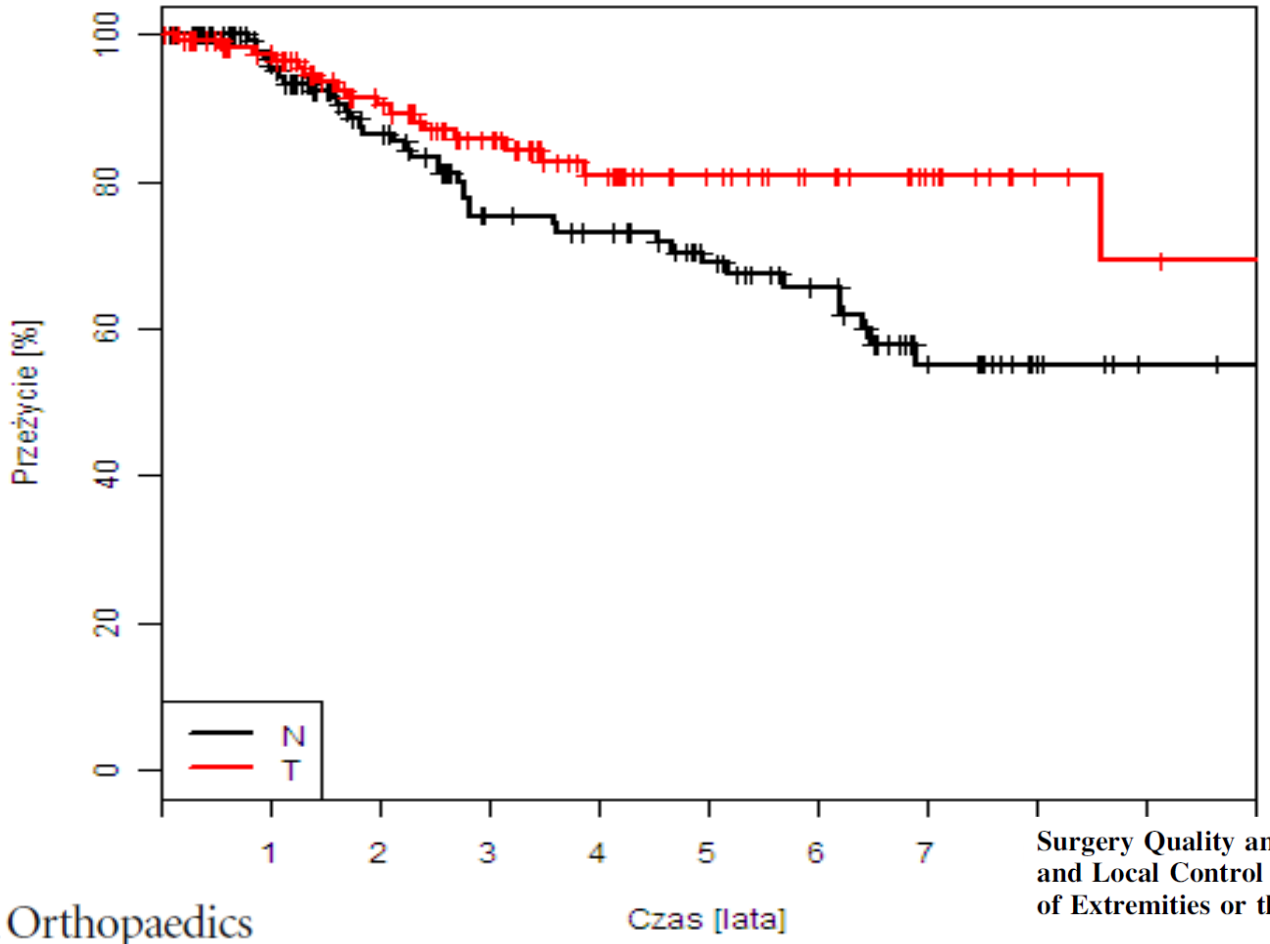
	5-year LRFS	95% CI
Unplanned excision and tumour bed re-excision	63.7%	50.7-75.1%
Primary planned excision	89.7%	83.1-94.0%
P-value	P<0.0001	

Unplanned excisions of high-grade STS resulted in increased rates of local recurrence but not disease-specific survival

CI, confidence interval; LRFS, local relapse-free survival; STS, soft tissue sarcoma

Potter B, et al. Clin Orthop Relat Res 2008;466:3093-100

OS (liposarcoma) according to preoperative biopsy



p=0.02

Clinical Orthopaedics and Related Research®
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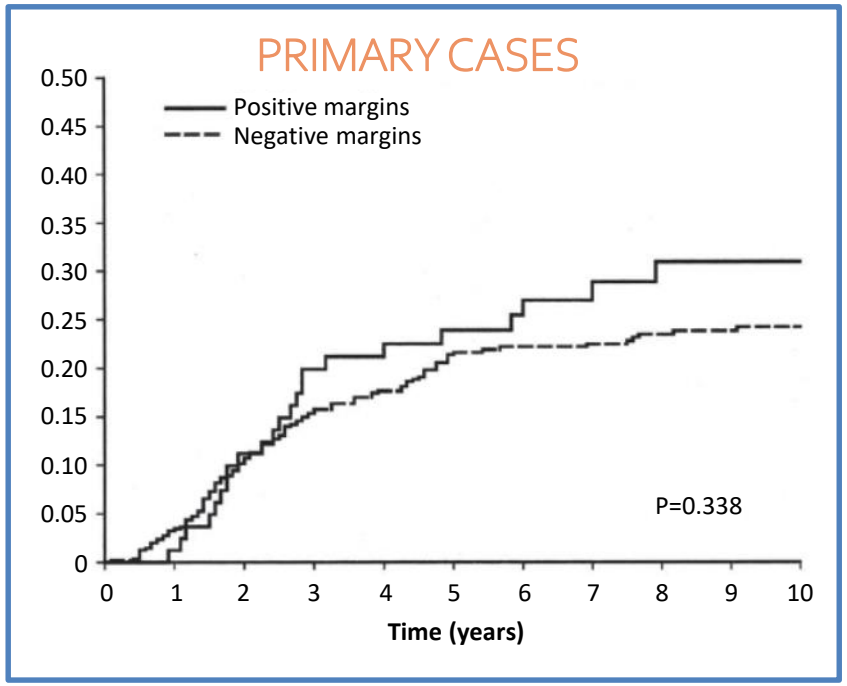
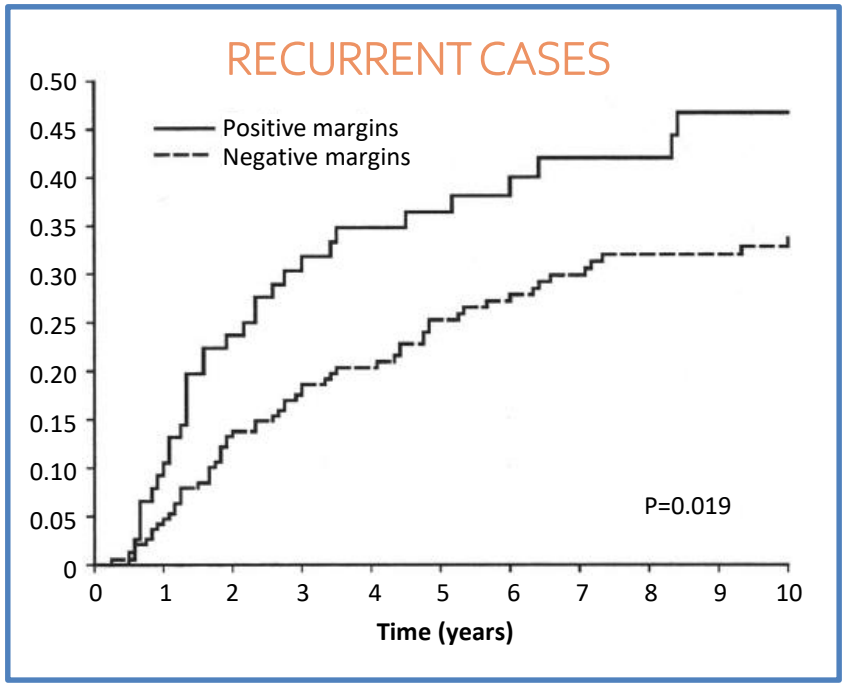
Surgery Quality and Tumor Status Impact on Survival and Local Control of Resectable Liposarcomas of Extremities or the Trunk Wall

Piotr Rutkowski MD, PhD, Sławomir Trepka MD, PhD,
Konrad Ptaszynski MD, PhD,
Milena Kołodziejczyk MD, PhD

Cause-specific mortality by microscopic margin status





10-year mortality Primary cases	HR	95% CI
Positive margin	0.31	0.20-0.42
Negative margin	0.24	0.20-0.28

10-year mortality Recurrent cases	HR	95% CI
Positive margin	0.47	0.34-0.59
Negative margin	0.34	0.26-0.41

CI, confidence interval; HR, hazard ratio

Gronchi A, et al. J Clin Oncol 2005;23:96-104

IMPORTANCE OF MultiDisciplinary Team (MDT)

The management of soft tissue sarcoma (STS) requires an organized, structured approach involving many disciplines

If an MDT is not utilized, a large proportion of patients with STS may be subject to an initial suboptimal surgery resulting in the need for more extensive surgery and radiation than the original tumor may dictate

Diagnosis of the primary lesion, distal metastasis, or subsequent local recurrence requires the use of **advanced imaging** (MRI +/- contrast, or CT for biopsy) as well as the expertise of appropriately trained **pathologists**

Surgeries, especially for wide re-excision after unplanned primary excision of soft tissue sarcoma, often require **plastic surgeons** for optimal tissue coverage

CT, computed tomography; MDT, multi-disciplinary team; MRI, magnetic resonance imaging; STS, soft tissue sarcoma

Siegel GW, et al. J Multidiscip Health 2015;8:109-15

Soft tissue and visceral sarcomas: ESMO–EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. G. Casali[1], N. Abecassis[2], S. Bauer[3], R. Biagini[4], S. Bielack[5], S. Bonvalot[6], I. Boukovinas[7], J. V. M. G. Bovee[8], T. Brodowicz[9], J. M. Broto[10], A. Buonadonna[11], E. De Álava[10], A. P. Dei Tos[12], X. G. Del Muro[13], P. Dileo[14], M. Eriksson[15], A. Fedenko[16], V. Ferraresi[17], A. Ferrari[18], S. Ferrari[19], A. M. Frezza[1], S. Gasperoni[20], H. Gelderblom[21], T. Gil[22], G. Grignani[23], A. Gronchi[1], A. Hannu[24], B. Hassan[25], P. Hohenberger[26], R. Issels[27], H. Joensuu[28], R. L. Jones[29], I. Judson[30], P. Jutte[31], S. Kaal[32], B. Kasper[26], K. Kopeckova[33], D. A. Krákorová[34], A. Le Cesne[35], I. Lugowska[36], O. Merimsky[37], M. Montemurro[38], M. A. Pantaleo[39], R. Piana[40], P. Picci[19], S. Piperno-Neumann[6], A. L. Pousa[41], P. Reichardt[42], M. H. Robinson[43], P. Rutkovski[26], A. A. Safwat[44], P. Schöffski[45], S. Sleijfer[46], S. Stacchiotti[47], K. Sundby Hall[48], M. Unk[49], F. Van Coevorden[50], W. Van der Graaf[29], J. Whelan[51], E. Wardelmann[52], O. Zaikova[53] & J. Y. Blay[54], on behalf of the ESMO Guidelines Committee and EURACAN*

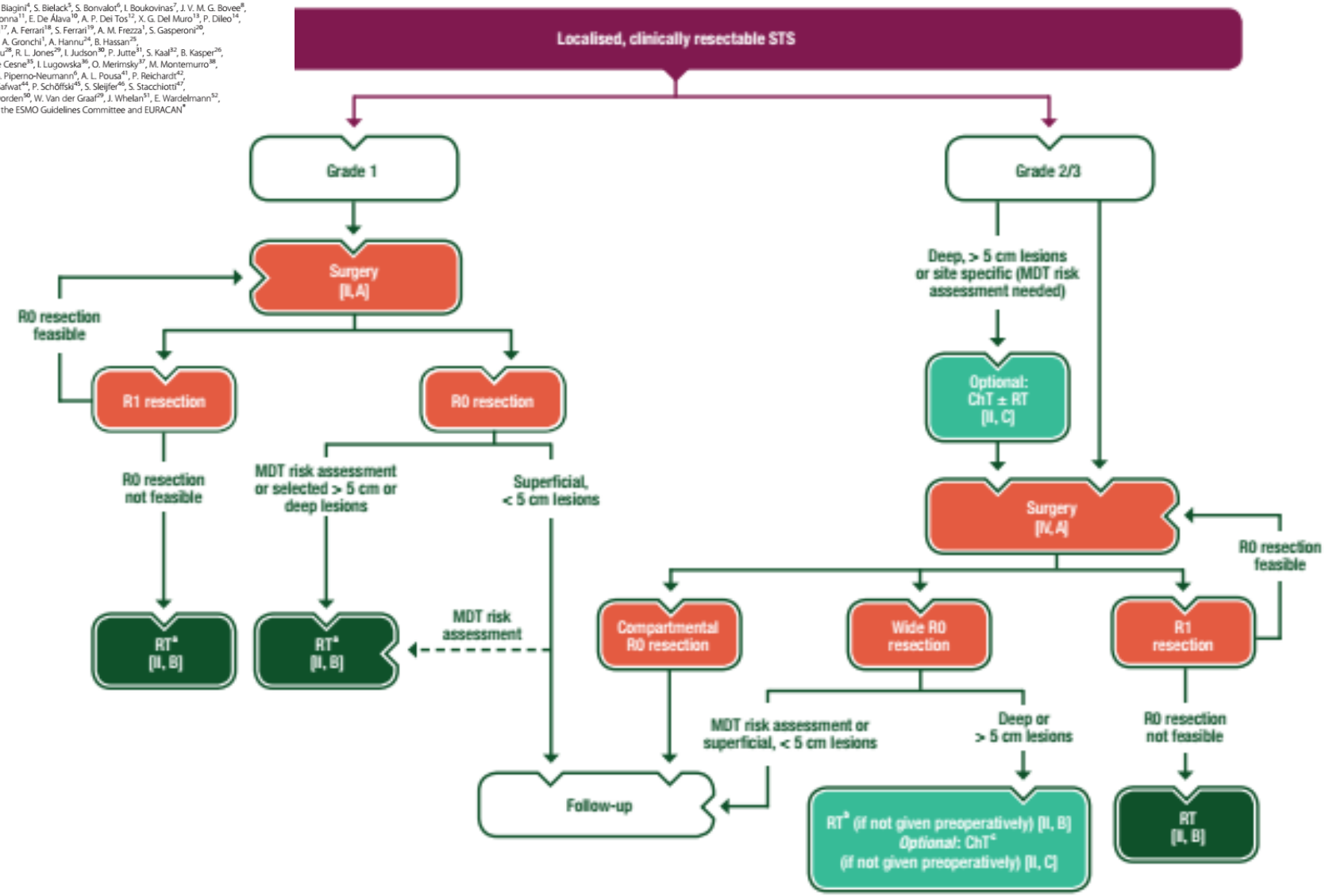


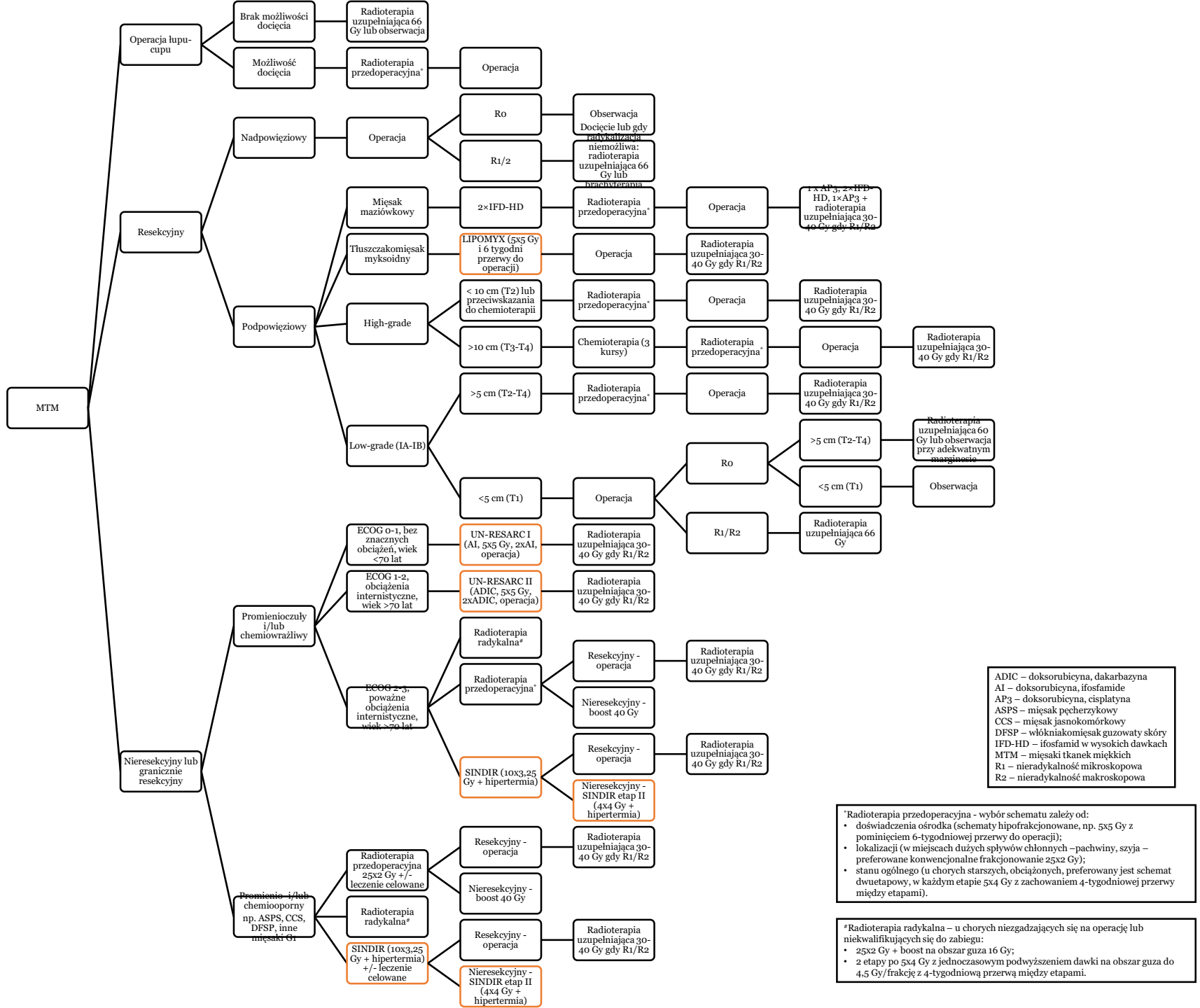
Figure 1. Management of localised, clinically resectable STS.

[a]RT can be omitted in selected cases; *optional*: isolated limb perfusion in highly selected cases.

[b]RT can be omitted in selected deep cases and added in selected superficial cases; to be administered preoperatively if problematic postoperatively.

[c]Extremity and superficial trunk, G3, deep, > 5 cm.

ChT, chemotherapy; MDT, multidisciplinary team; R0, no tumour at the margin; R1, microscopic tumour at the margin; RT, radiotherapy; STS, soft tissue sarcoma.

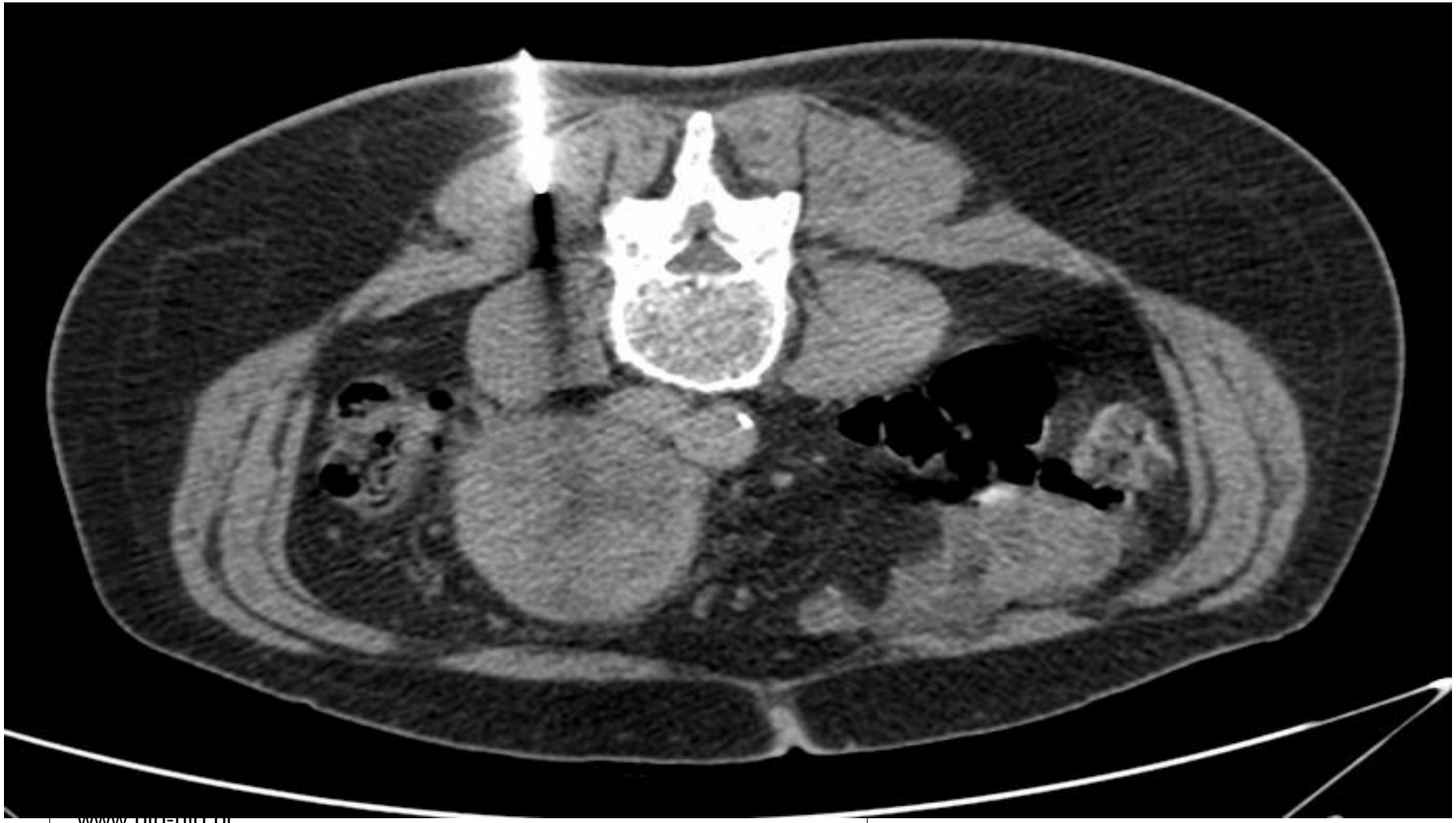


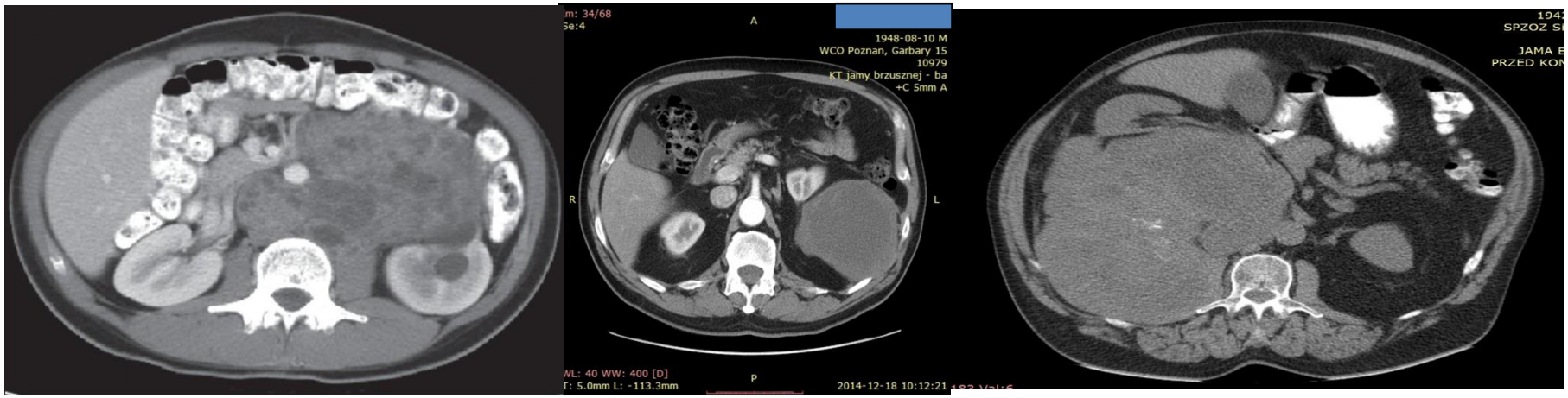
ADIC – doksorubicyna, dakarbazyna
AI – doksorubicyna, ifosfamide
AP3 – doksorubicyna, cisplatyna
ASPS – mięsak pęcherzykowy
CCS – mięsak jasnokomórkowy
DFSP – włókniakomięsak guzowaty skóry
IFD-HD – ifosfamid w wysokich dawkach
MTM – mięsaki tkanek miękkich
R1 – nieradykalność mikroskopowa
R2 – nieradykalność makroskopowa

*Radioterapia przedoperacyjna - wybór schematu zależy od:
- doświadczenia ośrodka (schematy hipofrakcjonowane, np. 5x5 Gy z pominięciem 6-tygodniowej przerwy do operacji);
- lokalizacji (w miejscach dużych spływów chłonnych –pachwiny, szyja – preferowane konwencjonalne frakcjonowanie 25x2 Gy);
- stanu ogólnego (u chorych starszych, obciążonych, preferowany jest schemat dwuetapowy, w każdym etapie 5x4 Gy z zachowaniem 4-tygodniowej przerwy między etapami).

#Radioterapia radykalna – u chorych niezgadzających się na operację lub niekwalifikujących się do zabiegu:
- 25x2 Gy + boost na obszar guza 16 Gy;
- 2 etapy po 5x4 Gy z jednoczasowym podwyższeniem dawki na obszar guza do 4,5 Gy/frakcję z 4-tygodniową przerwą między etapami.

Retroperitoneal sarcomas

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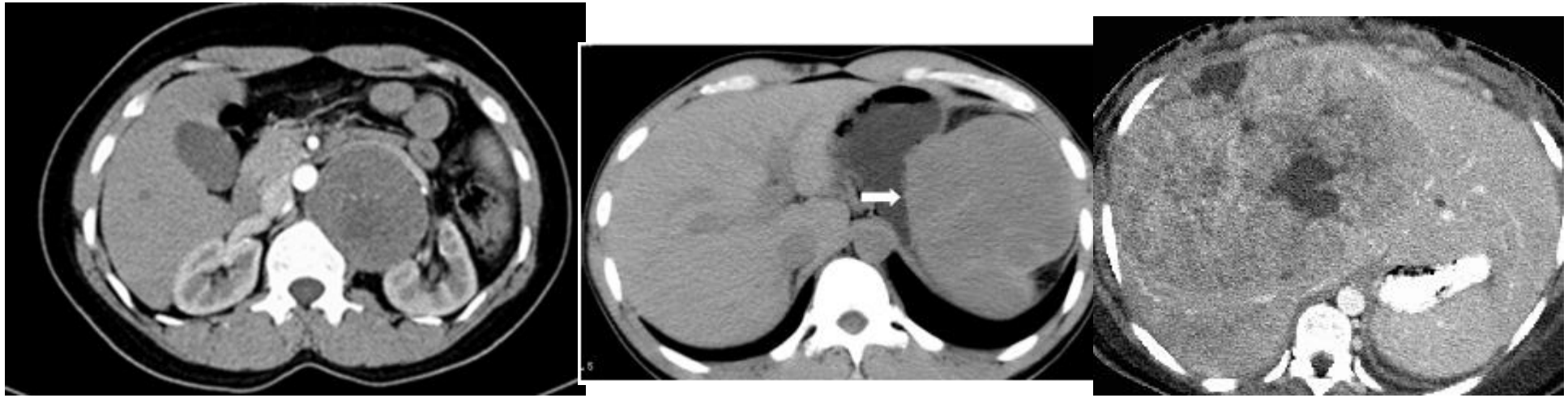
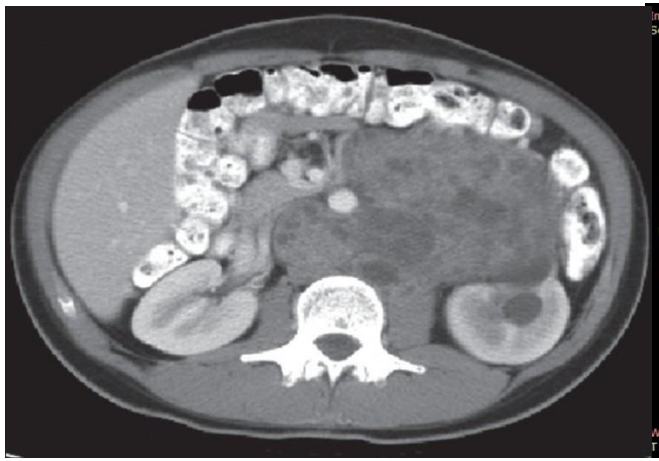
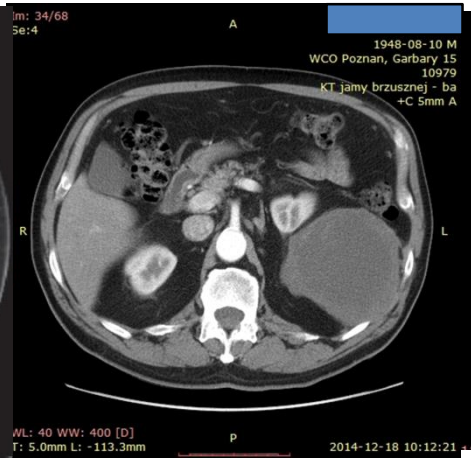


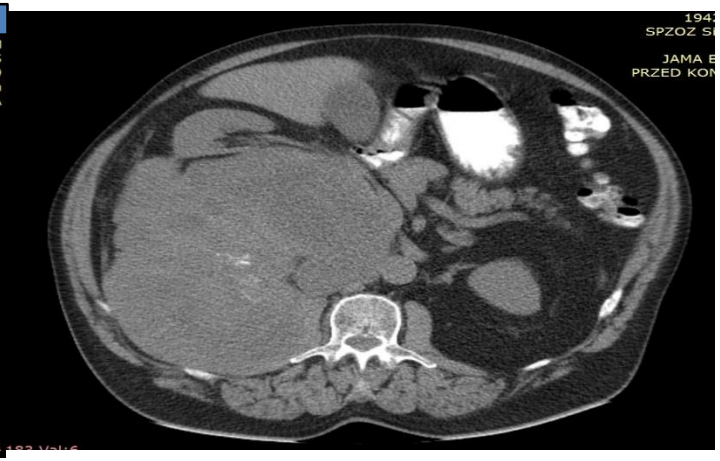
Chondrosarcoma of the rib

Germ cell tumor

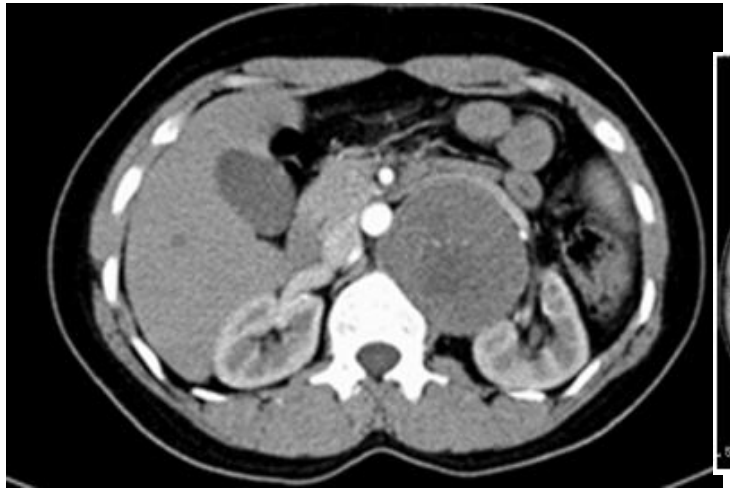




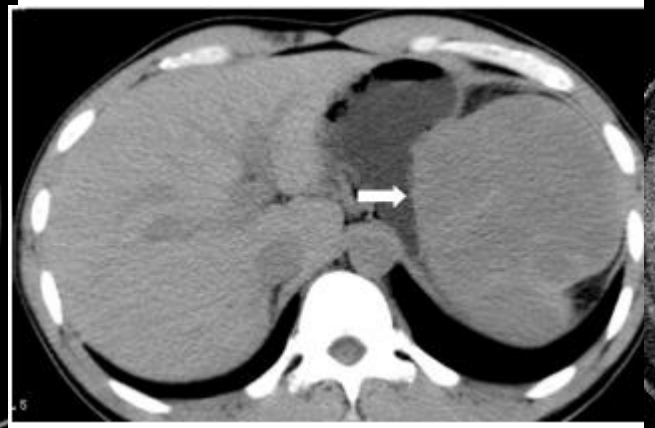
Dediff liposarcoma



Schwannoma



Lymphoma



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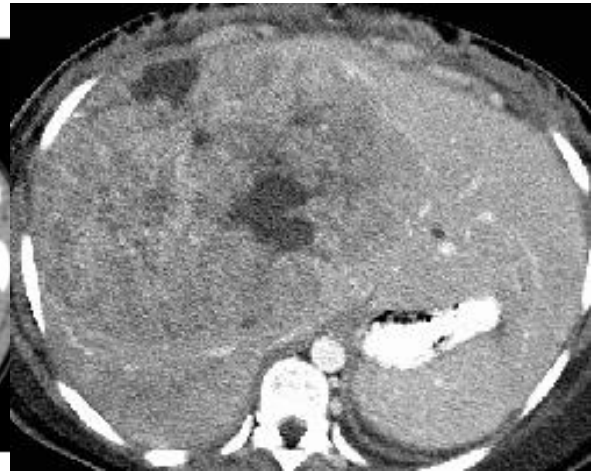

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Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – SARCOMA

Early and Late Complications of Percutaneous Core Needle Biopsy of Retroperitoneal Tumors at Two Tertiary Sarcoma Centers

David Berger-Richardson, MD[1,2], Sally M. Burtenshaw, MSc[3,4], Andrea M. Ibrahim, MSc[5], Rebecca A. Gladdy, MD[1,2,3,4], Rebecca Auer, MD[5,6,7], Rob Beecroft, MD[8], Brendan C. Dickson, MD[9], Bibianna Purgina, MD[10], Kristin Ambacher, MD[5], Carolyn Nessim, MD[5,6,7], and Carol J. Swallow, MD[1,2,3,4]

TABLE 2 Early complications after percutaneous CNB of a retroperitoneal mass (1999–2015)

	Total [*N* (%)] 358	Malignant [*N* (%)] 249	Benign/nondiagnostic [*N* (%)] 109
Patients with complications after CNB, total	11 (3.1)	4 (2)	7 (6)[b]
Bleed, minor[a]	7[c] (2.0)	3	4[c]
Bleed, major	0	0	0
Pain requiring analgesics	3[c] (0.8)	0	3[c]
Unplanned hospital admission, respiratory distress	1 (0.3)	1	0
Pneumothorax, asymptomatic	1 (0.3)	0	1
Infection	0	0	0

CNB core needle biopsy

[a]Requiring no intervention

[b]$p = 0.02$ versus malignant diagnoses, Chi square

[c]One patient with what proved to be a benign mass had both pain and minor bleeding

Narodowy Instytut Onkologii
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Państwowy Instytut Badawczy

Diagnostic accuracy of percutaneous biopsy in retroperitoneal sarcoma

BJS 2019; **106**: 395–403

L. M. Almond[1], F. Tirotta[3], H. Tattersall[1], J. Hodson[2], T. Cascella[4], M. Barisella[4], A. Marchianò[4], G. Greco[4], A. Desai[1], S. J. Ford[1], A. Gronchi[3], M. Fiore[3] and C. Morosi[4]

Table 2 Predictive accuracy of histology on biopsy compared with pathology on the resection specimen

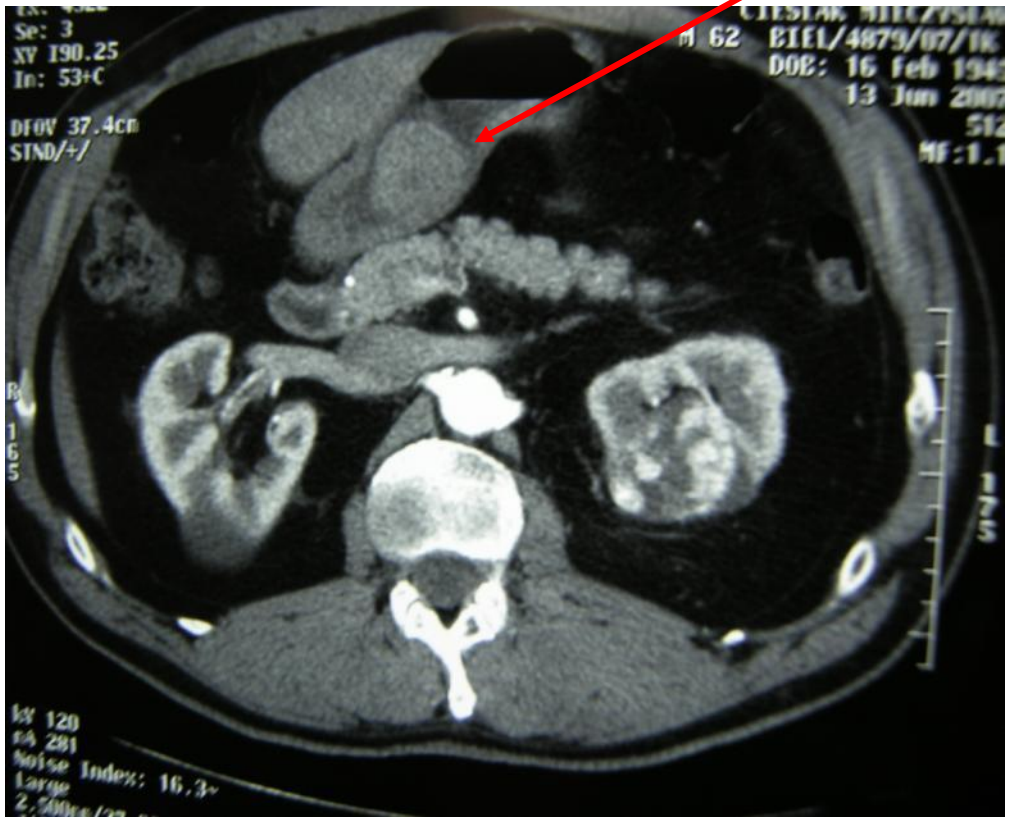
Histology on biopsy	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Liposarcoma combined*	85	97	96	87
DDLPS	40	99	97	76
WDLPS	95	82	49	99
Leiomyosarcoma	87	99	90	98
Indeterminate/other sarcoma	80	91	65	96
Other non-sarcoma malignancy	53	99	80	97
Benign tumour	77	96	77	96

*Diagnosis of sarcoma, either dedifferentiated liposarcoma (DDLPS) or well differentiated liposarcoma (WDLPS). PPV, positive predictive value; NPV, negative predictive value.

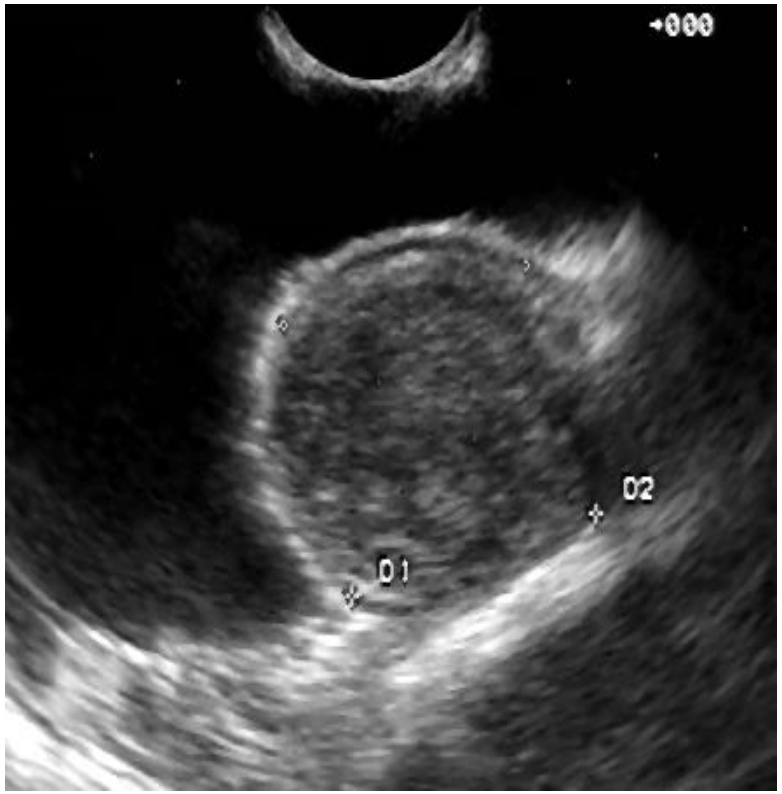
Results: A total of 239 patients underwent percutaneous core biopsy followed by surgical resection in Milan (163, 68·2 per cent) or Birmingham (76, 31·8 per cent). Diagnostic accuracy varied with histological diagnosis ($P < 0·001$), but demonstrated overall concordance with final pathology following resection in 67·2 per cent of biopsies ($\kappa = 0·606$). The majority of discrepancies occurred in dedifferentiated liposarcoma (DDLPS), owing to under-recognition of dedifferentiation in this group. Concordance between pathology on biopsy and resection improved to 81·1 per cent when DDLPS and well differentiated liposarcoma were grouped together as liposarcoma. Grade on biopsy was concordant with grade on resection specimen in 60·4 per cent of tumours ($\kappa = 0·640$). Diagnosis of high-grade tumours on biopsy had a high specificity (98 per cent), and moderate positive predictive value (85 per cent) and negative predictive value (78 per cent).

Conclusion: A diagnosis of DDLPS or leiomyosarcoma on percutaneous biopsy is highly reliable. High-grade sarcomas can be identified with high specificity, which opens the door to a study on neoadjuvant therapy in these patients.

GIST - diagnostics



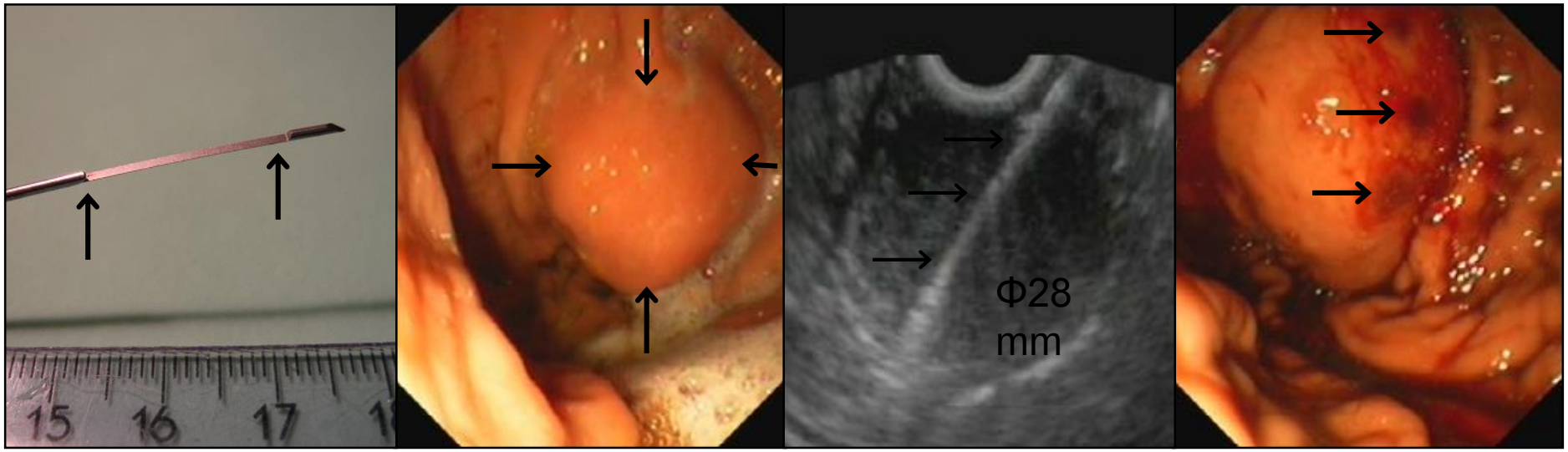
CT/MRI

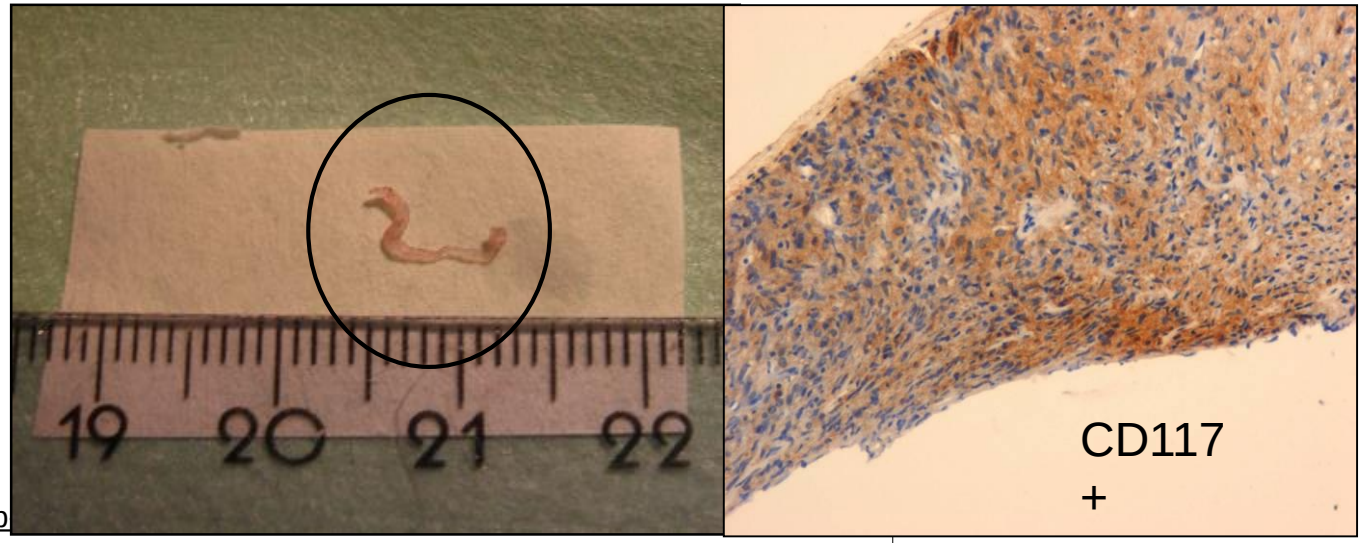


Endoscopy and EUS

Endoscopic or percutaneous biopsy

Core needle biopsy of gastric GIST





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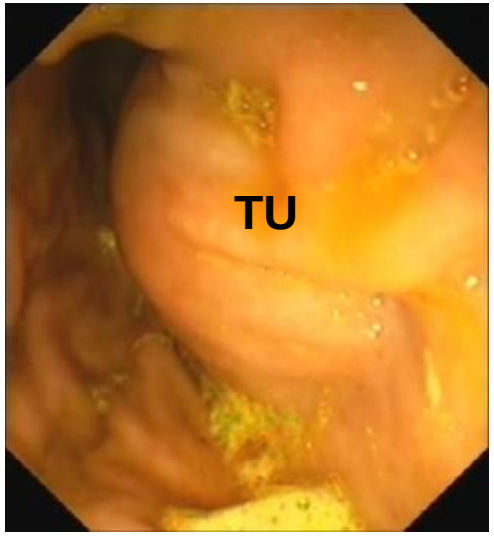
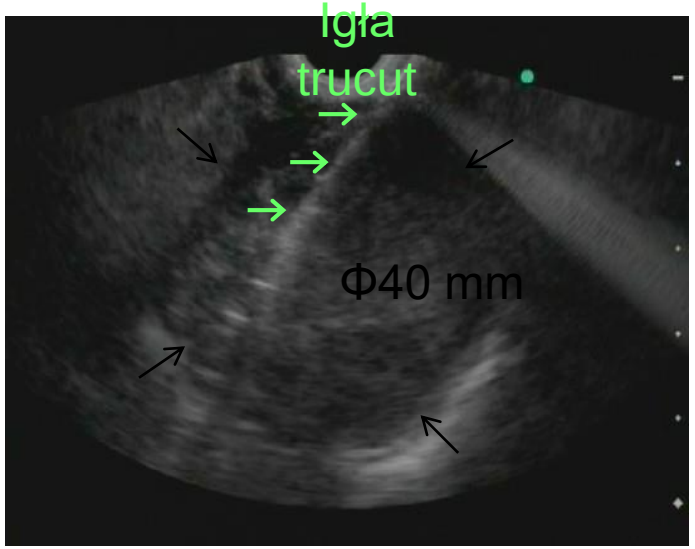
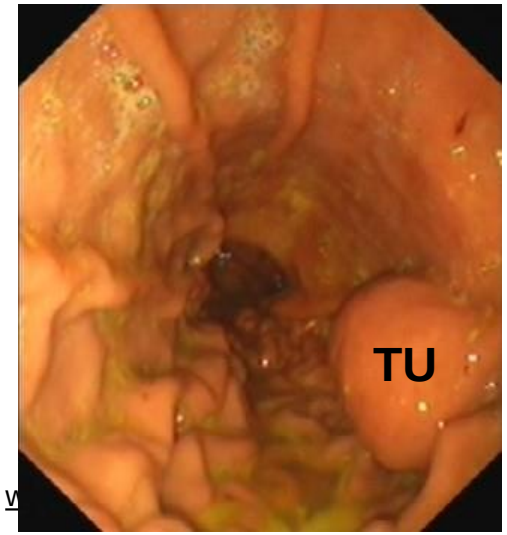
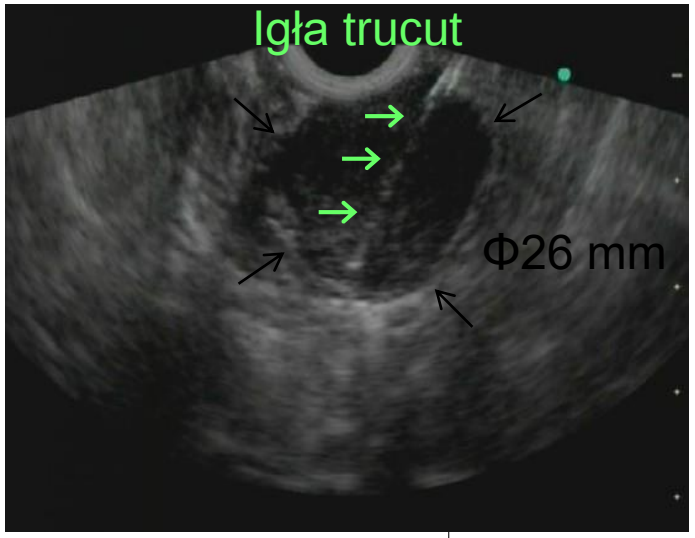
Impact of needle biopsy: resectable gastric tumors





GIST, CD117+
⇒ operation





Leiomyoma
in 80-yo patient

Diagnostic yield and safety of endoscopic-ultrasound guided trucut biopsy in patients with gastric submucosal tumors: a prospective study

Endoscopy

M. Polkowski[1,2], W. Gerke[1,2], D. Jarosz[1,2], A. Nasierowska-Guttmejer[3], P. Rutkowski[4], Z. I. Nowecki[4], W. Ruka[4], J. Regula[1,2], E. Butruk[1,2]

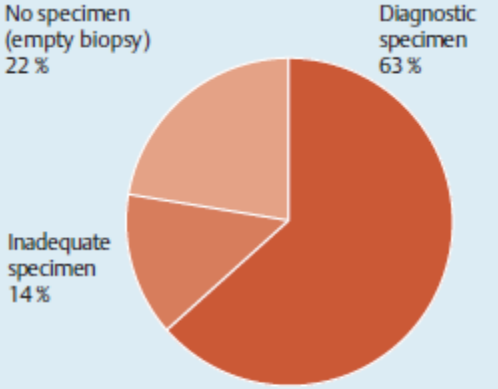
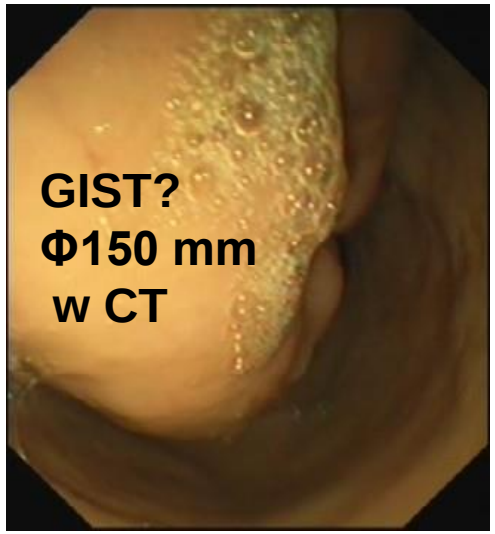
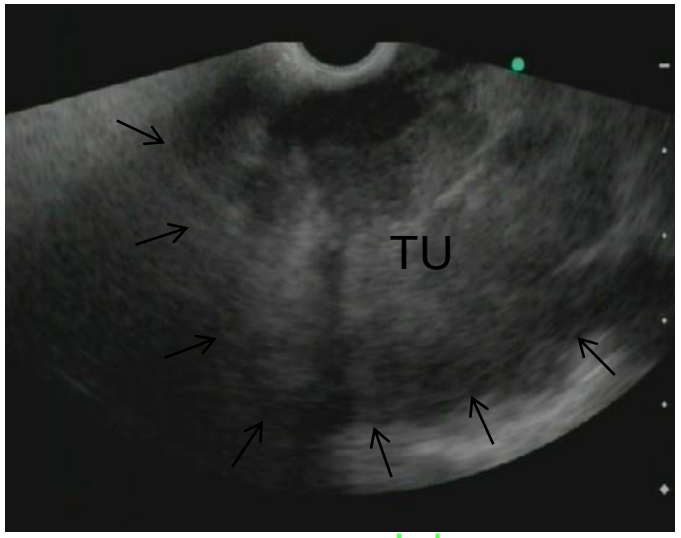


Fig. 1 Diagnostic yield of endoscopic ultrasonography-guided trucut biopsy of 49 gastric hypoechoic submucosal tumors at least 20 mm in size ("inadequate specimen" means that no tissue remained for immunostaining after hematoxylin and eosin staining had been performed). Values do not add to 100 % because of rounding.

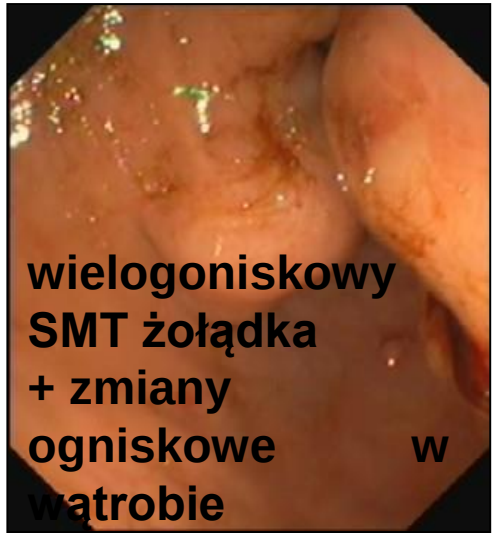
the success of the biopsy. Agreement between EUS-TCB and surgical pathology specimens in respect of the diagnosis and CD117 status was high (0.9, standard error 0.31; and 0.95, standard error 0.16, respectively); however, there was no correlation between the mitotic index as determined on EUS-TCB and that determined on the surgical pathology specimen (correlation coefficient,

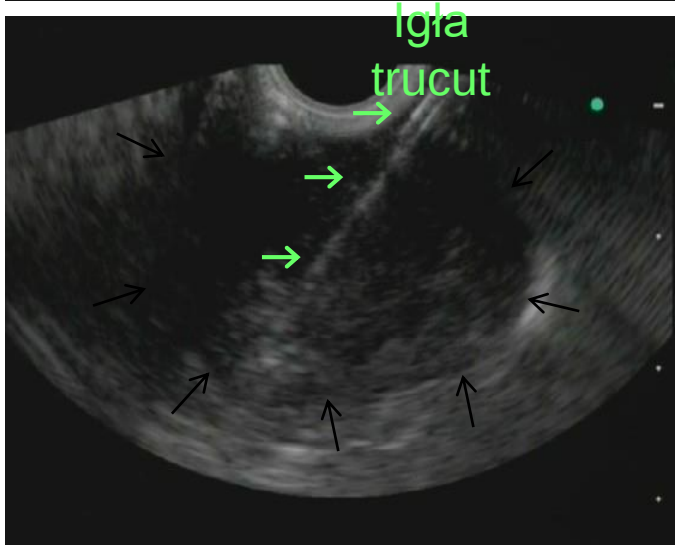
Impact of needle biopsy: unresectable gastric tumors





GIST, CD117+
⇒ Imatinib





GIST, CD117+
⇒ Imatinib

PRINCIPLES OF BIOPSY FOR GIST

- GISTs are soft and fragile tumors. EUS-FNA biopsy of primary site is preferred over percutaneous biopsy (due to the risk for hemorrhage and intra-abdominal tumor dissemination).
- Consideration of biopsy should be based on the suspected tumor type and extent of disease.
- Biopsy is necessary to confirm the diagnosis of primary GIST prior to the initiation of preoperative therapy.
- Percutaneous image-guided biopsy may be appropriate for confirmation of metastatic disease.
- Diagnosis is based on the Principles of Pathologic Assessment (See SARC-B); referral to centers with expertise in sarcoma diagnosis is recommended for cases with complex or unusual histopathologic features.
- Testing for mutations in *KIT* and *PDGFRA* is strongly recommended.
- Testing for germline mutations in the *SDH* genes should be considered for patients with wild-type GIST (lacking *KIT* or *PDGFRA* mutations).
- Risk stratification:
  - While tumor size and mitotic rate are used to assess the risk of metastasis of GIST, it is notoriously difficult to predict the biologic behavior of GIST based on pathologic features alone; thus, guidelines for risk stratification by tumor site have been developed.
  - Most gastric GISTs behave in an overall indolent manner and those smaller than 2 cm are almost universally benign. See Table 1: Gastric GISTs: Proposed Guidelines for Assessing the Malignant Potential (GIST-A 2 of 3).
  - GIST of the small intestine tends to be more aggressive than its gastric counterpart. See Table 2: Non-Gastric GISTs: Proposed Guidelines for Assessing Malignant Potential (GIST-A 3 of 3).
  - GIST of the colon is most commonly seen in the rectum; colonic GIST tends to have an aggressive biological behavior, and tumors with mitotic activity can recur and metastasize despite a small size of <2 cm.
  - Specific mutations in *KIT* or *PDGFRA* show some correlation with tumor phenotype, but mutations are not strongly correlated with the biologic potential of individual tumors. The accumulated data show that *KIT* mutations are not preferentially present in high-grade tumors, and can also be found in small incidental tumors as well as tumors that have a benign course. Similarly, mutational analysis of *PDGFRA* cannot be used to predict the behavior of individual tumors.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

The most important aspects of perioperative therapy of GIST

1. Diagnosis of GIST
2. Biopsy before any planned operation
3. MDT – plan of combined therapy
4. Therapy according to established plan

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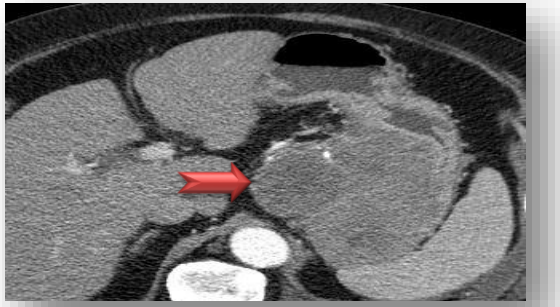
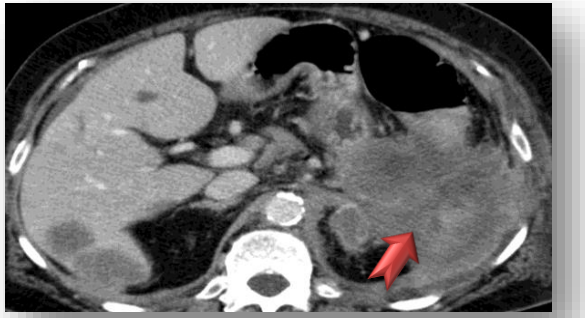
1. Diagnosis

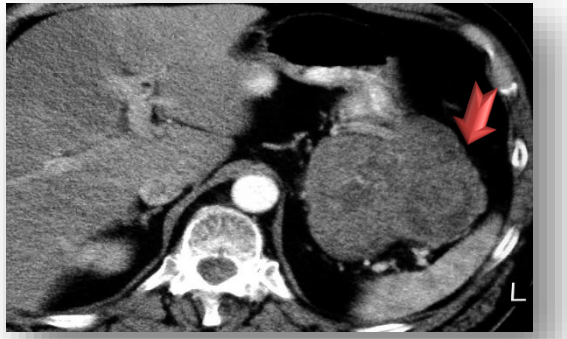
Choi YR Eur J Radiol 2014 , Scola D Abdom Radiol 2017



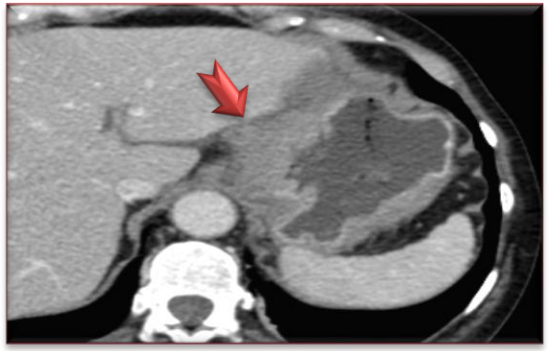
GIST



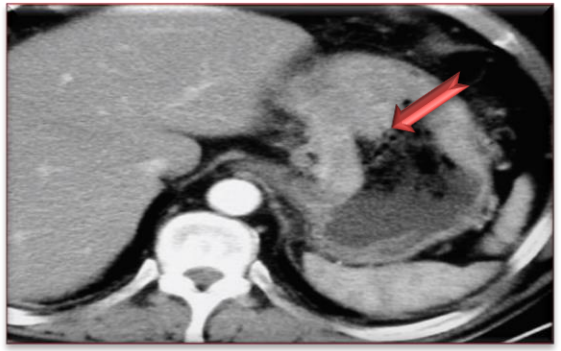
Adenocarcinoma



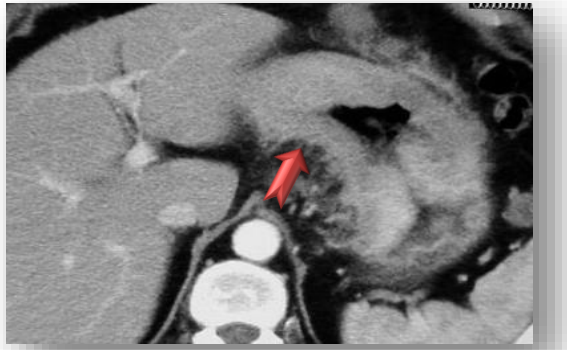
Leiomyosarcoma



Lymphoma



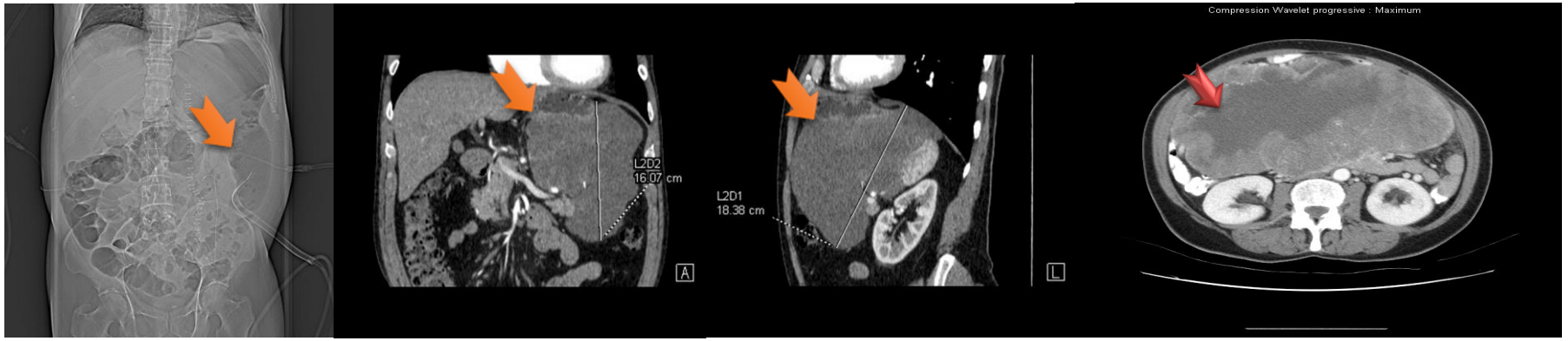
Breast carcinoma



Gastric linitis

2. Preoperative biopsy

- To confirm diagnosis
- To evaluate molecular profile



3. MDT – plan of combined therapy

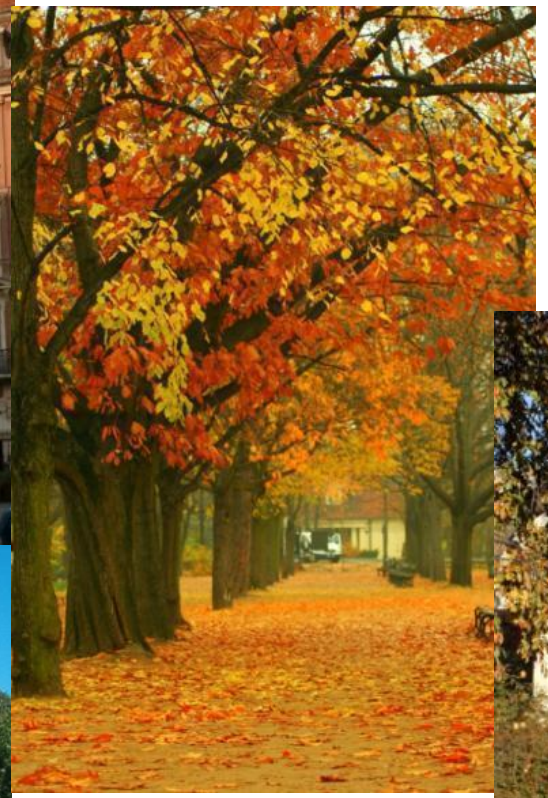
Good conditions for surgical resection **(no necessity for induction systemic therapy to decrease tumor extent) –** Surgery +/- postoperative therapy

If R0 surgery is not feasible, or it could be achieved through less mutilating/function-sparing surgery in the case of volumetric reduction -

- Preoperative imatinib should be considered

- Surgery after 6-12 months

- Adjuvant imatinib therapy (till 3 years in total)



Thank you for your attention!

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Department of Soft Tissue/Bone Sarcoma and Melanoma

Piotr Rutkowski

Surgery
Tomasz Goryń
Andrzej Pieńkowski
Maciej Sałamacha
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Beata Mitręga-Korab
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Jacek Skoczylas
Bartosz Szostakowski
Konrad Zaborowski
Maria Krotewicz
Kamila Jakubiak

Medical oncology
Hanna Koseła-Paterczyk
Sławomir Falkowski
Tomasz Świtaj
Katarzyna Kozak
Anna Klimczak
Iwona Ługowska
Paweł Rogala
Paulina Jagodzińska-Mucha
Paweł Teterycz
Monika Dudzisz-Śledź
Anna M. Czarnecka
Joanna Placzke
Paweł Sobczuk

Radiotherapy
Tadeusz Morysiński
Aneta Borkowska
Mateusz Spałek

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