# Metastatický renální karcinom

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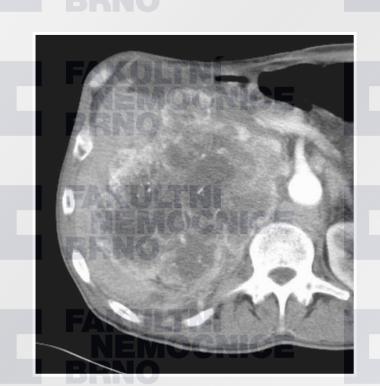
### Renální karcinom

- 25-30 % v metastatickém stádiu
- 40 % pacientů má metastázy v průběhu sledovaní po léčbě primárního ložiska
- incidence recidivy většinou do 3 let od operace
- Incidence stoupá s věkem od 50 let

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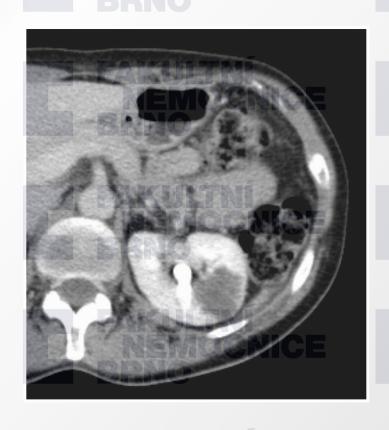
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### Recidíva a metastázy

Tendence k metastazování - velikost, histologie, podíl nekróz

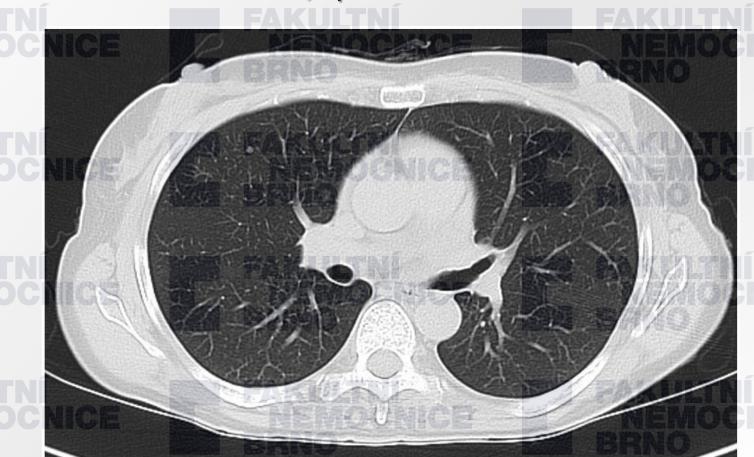
- < 3 cm 2,5 %
- 3-5 cm 15,4 %
- > 5 cm 78 %



- po nefrektomii relaps u 20 30 %
  medián relapsu do 1,2 let,
  ( 90% do 3 let)
- kasuistické případy metastáz i po více než 30 letech
- metastázy imitují charakter primárního ložiska
   hypervaskularizace v 65-75%
- růst primárního tumoru 0,54 cm za rok růst metastázy 1,72 cm za rok (0,08-8cm)

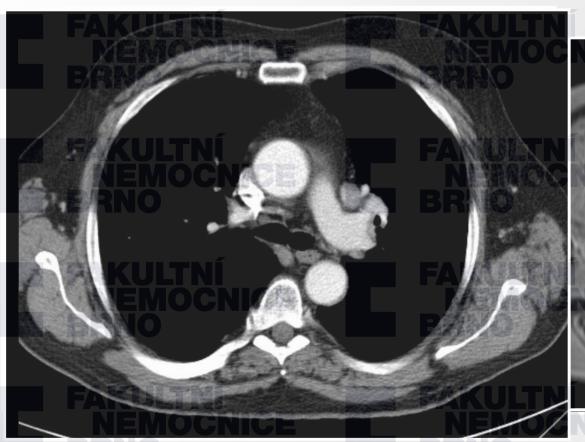
### Plice

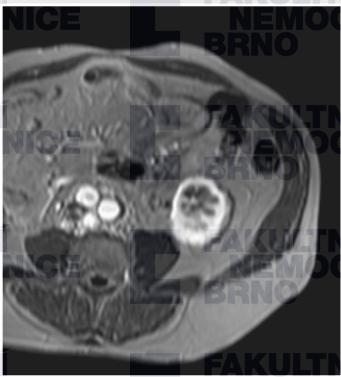
- s incidencí 55% je to nejčastější místo metastáz,
- v 32 % je to jediné místo metastáz
- positivita FDG-PET 71,4%
- 1-5mm 23,5%, >25mm 88,5% Fortes 2008, Eur J Cardiothorac Surg
- FDG-PET/CT sensitivita až 100%, specificita ale nízká



## Lymfatické uzliny

- 2. nejčastější místo metastáz (34%)
- jen v 12 % je to jediné místo metastáz retroperitoneum
- v 66 % pacientů s metastázami nejčastější kombinace plíce a uzliny uzliny paratracheálně





# Kombinace oboustranné lymfadenopatie a plicních ložisek

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#### Chest

Volume 85, Issue 4, April 1984, Pages 533-536



Metastatic Renal Cell Carcinoma Simulating Sarcoidosis: Analysis of 12 patients with Bilateral Hilar Lymphadenopathy

Kesavan Kutty M.D., F.C.C.R a A, Basil Varkey M.D., F.C.C.P. a

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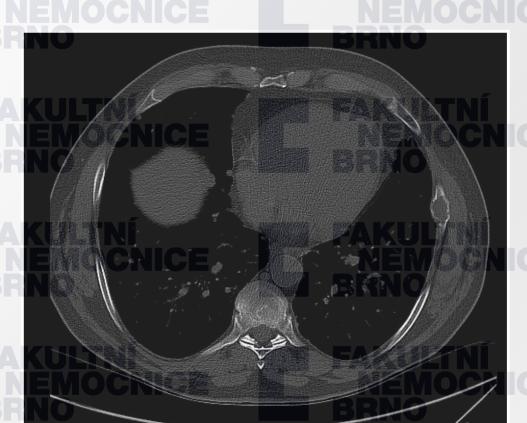
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### Skelet

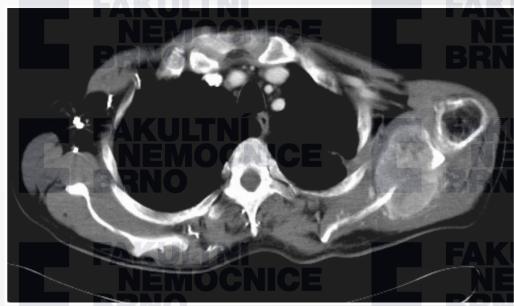
- 3. nejčastější místo metastáz (32%)
- jen v 9 % je to jediné místo metastáz
- v 42 % pacientů s metastázami
- TH, žebra 24 %
- L, pánev, femor





### Skelet

- 3. nejčastější místo metastáz (32%)
- jen v 9 % je to jediné místo metastáz
- v 42 % pacientů s metastázami
- TH, žebra 24 %
- L, pánev, femor





### Problém detekce okultních metastáz skeletu

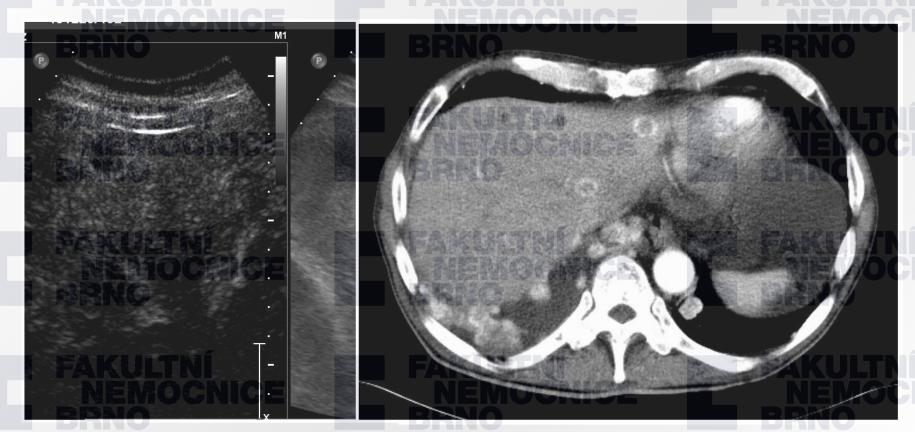
 kostní léze dominantně osteolytické s nízkou aktivitou osteoblastů - nízka míra detekce na scintigrafii skeletu

Sensitivita CT 46% a <sup>99m</sup>Tc-MDP scintigrafie jen 29%, kombinace 65%

Gerety 2015, Ann Oncol

### **Játra**

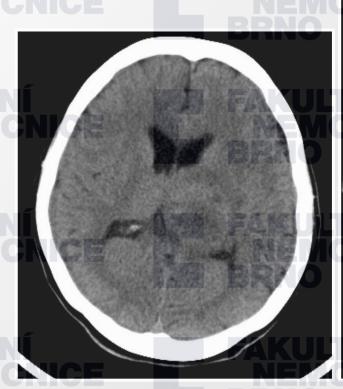
- jen v 6 % je to jediné místo metastáz
- v 41 % pacientů s metastázami
- přítomnost jaterních metastáz zhoršuje prognózu pacienta

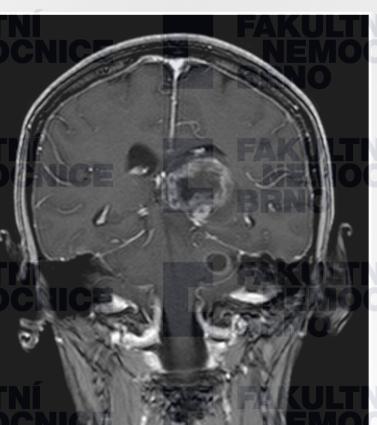


### Mozek

- **7**%
- 80% 90% symptomatický pacient
- (bolesti hlavy, zmatenost, změny chování)
- náchylný k spontánnímu







Mozek

- **7**%
- 80% 90% symptomatický pacient

# ! u rizikových skupin i asymptomatický pacienti s následným stereotaktickým zářením

J Neurooncol. 1995;23(3):253-6.

High incidence of asymptomatic brain lesions in metastatic renal cell carcinoma.

Seaman EK1, Ross S, Sawczuk IS.

Author information

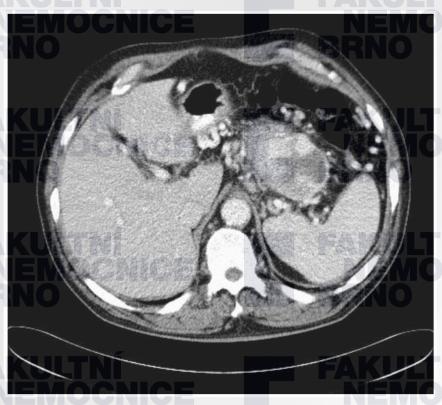
#### **Abstract**

The metastatic pattern of renal cell carcinoma has been well established. Studies have revealed a relatively high incidence of spread to lung, liver, bone and brain. A retrospective review of the records of ninety patients with metastatic renal cell carcinoma showed seven to have evidence of brain metastases. Six of the seven were asymptomatic at time of diagnosis. This study shows a significant incidence of asymptomatic brain metastases in patients with metastatic renal cell carcinoma. Subsequent to our chart review, an additional two patients have presented to our institution with asymptomatic brain lesions from metastatic renal cell carcinoma.

### **Pankreas**

- 14 % celkově
- jediné místo metastázy jen v 1%
- průměrný čas dg. 120 měsíců u poloviny pacientů tak více než 10 let





# Fázování kontrastní látky







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### Sensitivita PET

- primární nádor nízká senzitivita (exkrece FDG a malý počet GLUT-1 transporterů)
- rekurence resp. metastatický sensitivita 64-90%, specificita 71-100%

Park 2008, Majhail 2003, Nakatani 2011

▶ 18F-FDG PET vs CT přesnost 94% vs 89%

Aide 2003 Eur J Nucl Med Mol Imaging

dle metaanalýzy 18F-FDG PET nebo PET/CT vysoká sensitivita 86% (95% CI, 88-93%) a vysoká specificita 88% (95% CI, 84-91%) s výhodou detekce vzdálených metastáz

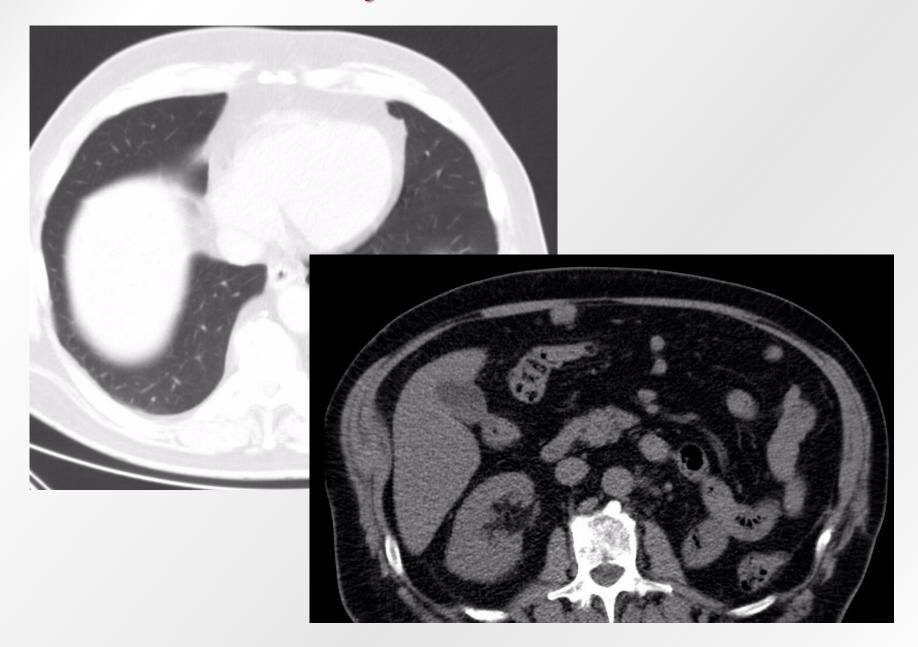
Ma 2017 Nucl Med Commun. 2017

### Jiné lokality

 nadledvina, kůže a podkoží, močový měchýř, uretery, kontralaterální ledvina, srdce, střevo



# Pacient s ca ledviny



# Pacient s ca ledviny

Dist 2.46 cm Dist 1.11 cm

2D 51% Dyn R 55 P Low Res



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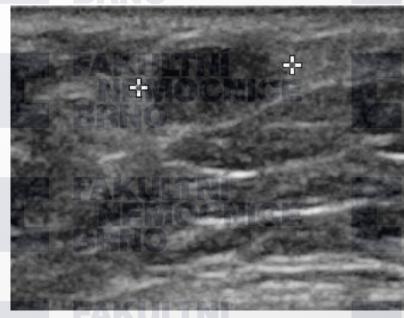
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# US, color doppler US

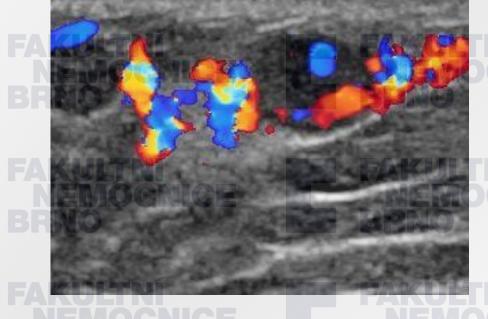
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Postgrad Med. 1992 May 15;91(7):145-6.

Metastatic renal cell carcinoma presenting as a breast mass.

Lesho EP1.

Author information

#### Abstract

Metastasis o importance c techniques ir

Am J Otolaryngol. 2004 Jan-Feb;25(1):54-7.

Metastatic renal cell carcinoma to the nasal cavity.

Nason R1, Carrau RL.

Arch Neurol. 2012 Jun;69(6):780-1. doi: 10.1001/archneurol.2011.500.

Metastatic renal cell carcinoma with radiologic appearance of a meningioma.

Jadhav AP1, Greenberg SA.

Saudi J Kidney Dis Transpl. 2013 Jan;24(1):100-4.

Metastatic renal cell carcinoma of gall bladder.

Jain D1, Chopra P.

Chin Med J (Engl). 2013;126(9):1793.

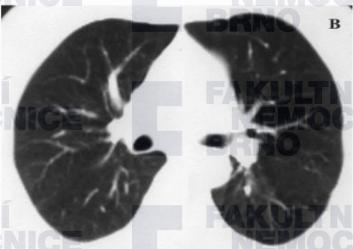
Metastatic renal cell carcinoma to vagina and review of literature.

Sun DQ, Lu JJ, Cao QW, Zhang H, Tian YJ, Bi DB, Ding ST.

## Abskopální efekt

- poprvé popsáno v roce 1928 Bumpus
- incidence není známá, míň než 1% případů
- dle literatury 90% regrese v plicích
- imunitně mediovaná reakce (nejen po chirurgii, ale i po ablacích, radioterapii a embolizaci)





CASE REPORT

Taylor & Francis
healthsciences

Spontaneous Regression of Pleural Metastases after Nephrectomy for Renal Cell Carcinoma

A Histologically Verified Case with Nine-year Follow-up

Asgeir Thoroddsen,<sup>1</sup> Tomas Gudbjartsson,<sup>1,4</sup> Gudmundur Geirsson,<sup>1,5</sup> Bjarni A. Agnarsson<sup>2,5</sup> and Kjartan Magnusson<sup>3</sup>

## Sledování pacientů po resekcích

- follow up během prvních 3 let kdy se objeví nejvíc metastáz
- stratifikace pacientů dle rizika (nízké, střední, vysoké) dle stádia, velikosti primárního tumoru, regionálních lymfatických uzlin, gradu ..
- nízké a střední riziko každých 6měsícu po dobu
   2let a následně kontroly ročně
- vysoké riziko každé 4 měsíce po dobu 2 let,
   6měsíců po dobu 5 let a dál ročně.

### Hodnocení odpovědi na léčbu

- ▶ 1979 WHO -
  - 1. pokus o standardizaci hodnocení odpovědi na léčbu
- ▶ 1999 RECIST 1.0
- ▶ 2009 RECIST 1.1

P. Therasse et. al. New Guidelines to Evaluate the Response to Treatment in Solid Tumors *JNCI J Natl Cancer Inst* (2000) 92(3): 205-216

#### SPECIAL ARTICLE

#### New Guidelines to Evaluate the Response to Treatment in Solid Tumors

Patrick Therasse, Susan G. Arbuck, Elizabeth A. Eisenhauer, Jantien Wanders, Richard S. Kaplan, Larry Rubinstein, Jaap Verweij, Martine Van Glabbeke, Allan T. van Oosterom, Michaele C. Christian, Steve G. Gwyther

Anticancer cytotoxic agents go through a process by which their antitumor activity—on the basis of the amount of tumor shrinkage they could generate—has been investigated. In the late 1970s, the International Union Against Cancer and the World Health Organization introduced specific criteria for the codification of tumor response evaluation. In 1994, several organizations involved in clinical research combined forces to tackle the review of these criteria on the basis of the experience and knowledge acquired since then. After several years of intensive discussions, a new set of guidelines is ready that will supersede the former criteria. In parallel to this initiative, one of the participating groups developed a model by which response rates could be derived from unidimensional measurement of tumor lesions instead of the usual bidimensional approach. This new concept has been largely validated by the Response Evaluation Criteria in Solid Tumors Group and integrated into the present guidelines. This special article also provides some philosophic background to clarify the various purposes of response evaluation. It proposes a model by which a combined assessment of all existing lesions, characterized by target lesions (to be measured) and nontarget lesions, is used to extrapolate an overall response to treatment. Methods of assessing tumor lesions are better codified, briefly within the guidelines and in more detail in Appendix I. All other aspects of response evaluation have been discussed, reviewed, and amended whenever appropriate. [J Natl Cancer Inst 2000; 92:205-16]

#### A. PREAMBLE

Early attempts to define the objective response of a tumor to an anticancer agent were made in the early 1960s (1,2). In the mid- to late 1970s, the definitions of objective tumor response were widely disseminated and adopted when it became apparent that a common language would be necessary to report the results of cancer treatment in a consistent manner.

The World Health Organization (WHO) definitions published in the 1979 WHO Handbook (3) and by Miller et al. (4) in 1981 have been the criteria most commonly used by investigators around the globe. However, some problems have developed with the use of WHO criteria: 1) The methods for integrating into response assessments the change in size of measurable and "evaluable" lesions as defined by WHO vary among research groups, 2) the minimum lesion size and number of lesions to be

recorded also vary, 3) the definitions of progressive disease are related to change in a single lesion by some and to a change in the overall tumor load (sum of the measurements of all lesions) by others, and 4) the arrival of new technologies (computed tomography [CT] and magnetic resonance imaging [MRI]) has led to some confusion about how to integrate three-dimensional measures into response assessment.

These issues and others have led to a number of different modifications or clarifications to the WHO criteria, resulting in a situation where response criteria are no longer comparable among research organizations—the very circumstance that the WHO publication had set out to avoid. This situation led to an initiative undertaken by representatives of several research groups to review the response definitions in use and to create a revision of the WHO criteria that, as far as possible, addressed areas of conflict and inconsistency.

In so doing, a number of principles were identified:

- 1) Despite the fact that "novel" therapies are being developed that may work by mechanisms unlikely to cause tumor regression, there remains an important need to continue to describe objective change in tumor size in solid tumors for the foreseeable future. Thus, the four categories of complete response, partial response, stable disease, and progressive disease, as originally categorized in the WHO Handbook (3), should be retained in any new revision.
- 2) Because of the need to retain some ability to compare favorable results of future therapies with those currently available, it was agreed that no major discrepancy in the meaning and the concept of partial response should exist between the old and the new guidelines, although measurement criteria would be different.
- 3) In some institutions, the technology now exists to determine

Affiliation: of authors: P. Therasse, J. Verweij, M. Van Giabbeke, A. T. van Oosteom, European Organization for Research and Treatment of Cancer, Brussels, Belgium; S. G. Arbuck, R. S. Kaplan, L. Rubinstein, M. C. Christian, National Cancer Institute, Betheeda, MD; E. A. Etienhauer, National Cancer Institute of Canada Clinical Trials Group, Kingston, ON, Canada, J. Wanders, New Drug Development Office Oncology, Amsterdam, The Netherlands; S. G. Gwruher, East Surger Healthcare National Health Service Trust, Reshill, U. M.

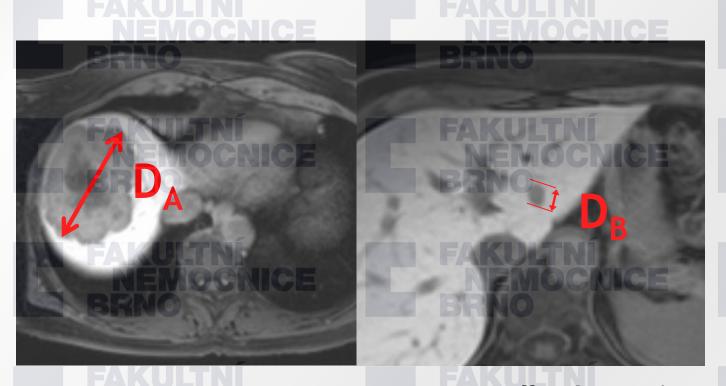
Correspondence to: Patrick Therasse, M.D., European Organization for Research and Treatment of Cancer Data Center, Avenue Mounier 83/11, 1200 Brussels, Belgium (e-mail: pth@eortc.be).

See "Note" following "References."

Oxford University Press

# RECIST 1.0 (1.1), iRECIST, irRECIST - pseudoprogrese

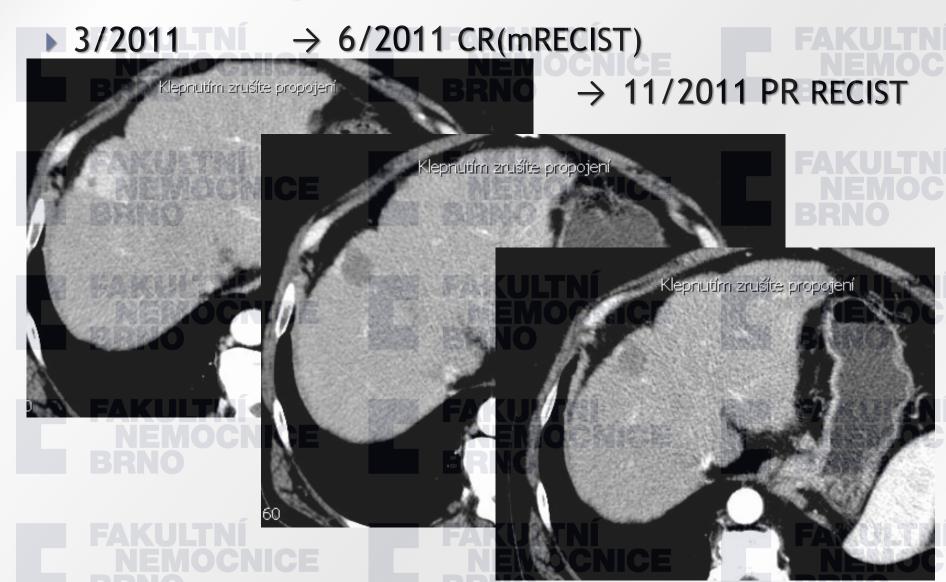
Response Evaluation Criteria In Solid Tumours



- Meření v jednom rozměru
- Maximálně 10 (5) target lézí
- Maximálně 5 (2) lézí/orgán

$$D_{\text{sum}} = D_{A} + D_{B}$$

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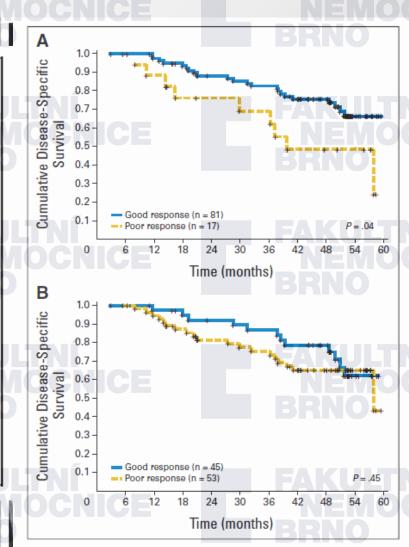
## Choi kritéria pro GIST

Response	Definition FAX
CR	Disappearance of all lesions
	No new lesions
PR	A decrease in size* of ≥ 10% or a decrease in tumor density (HU) ≥ 15% on CT
	No new lesions
	No obvious progression of nonmeasurable disease
SD	Does not meet the criteria for CR, PR, or PD
	No symptomatic deterioration attributed to tumor progression
PD	An increase in tumor size of ≥ 10% and does not meet criteria of PR by tumor density (HU) on CT
	New lesions
	New intratumoral nodules or increase in the size of the existing intratumoral nodules

Abbreviations: CR, complete response; PR, partial response; HU, Hounsfield unit; CT, computed tomography; SD, stable disease; PD, progression of disease; RECIST, Response Evaluation Criteria in Solid Tumors.

\*The sum of longest diameters of target lesions as defined in RECIST. 10

Benjamin RS, Choi H et al.
We should desist using RECIST, at least in GIST.
J Clin Oncol. 2007 May 1;25(13):1760-4.



**Fig 5.** Disease-specific survival in good and poor responders in the entire group of 98 patients by response criteria. (A) Response by Choi criteria; (B) response by Response Evaluation Criteria in Solid Tumors (RECIST). When the tumor response was evaluated on the basis of Choi response criteria, a significant difference was observed in disease-specific survival between the good and poor responders (P = .04) with follow-up to 60 months, but no significant difference was observed between good and poor responders by RECIST (P = .45).

# Revised Choi kritéria

<u>.</u>	

Table 3. Modified	CT	Response	Evaluation	Criteria
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Disappearance of all lesions

No new lesions

PR A decrease in size\* of ≥ 10% or a decreas density (HU) ≥ 15% on CT

No new lesions

No obvious progression of nonmeasurable

Does not meet the criteria for CR, PR, or PD SD No symptomatic deterioration attributed to tumor

progression An increase in tumor size of ≥ 10% and does not meet

Definition

criteria of PR by tumor density (HU) on CT New Jesions

New intratumoral nodules or increase in the size of the existing intratumoral nodules

Abbreviations: CR, complete response; PR, partial response; HU, Hounsfield unit; CT, computed tomography; SD, stable disease; PD, progression of disease; RECIST, Response Evaluation Criteria in Solid Tumors.

\*The sum of longest diameters of target lesions as defined in RECIST. 10

≥10% decrease in the sum of diameters of target lesions and ≥15% decrease in the tumor density or in patients with no lesions suitable for density analysis, ≥30% decrease in the sum of diameters of target lesions

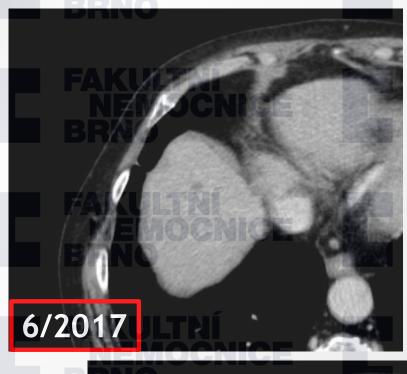
Benjamin RS, Choi H et al.

Response

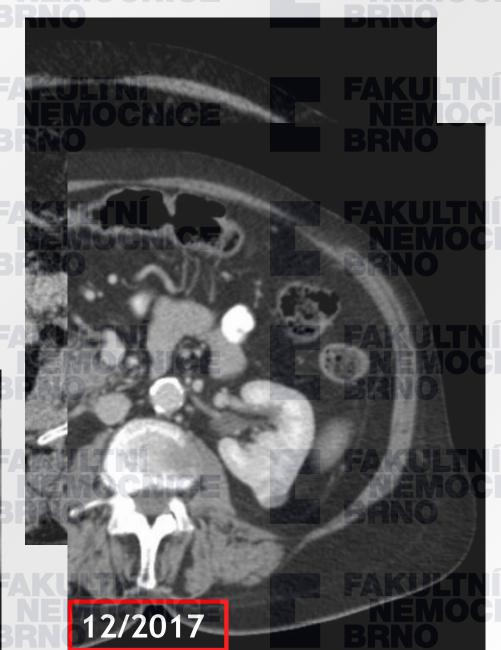
PD

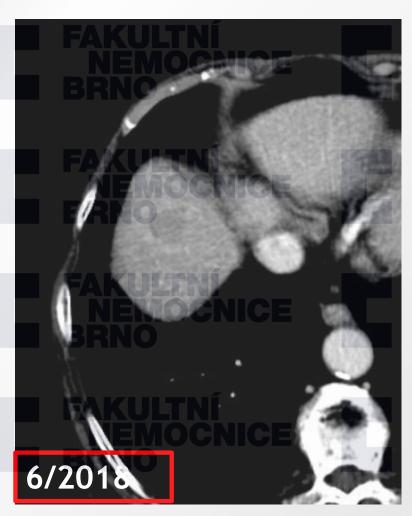
We should desist using RECIST, at least in GIST.

J Clin Oncol. 2007 May 1;25(13):1760-4.









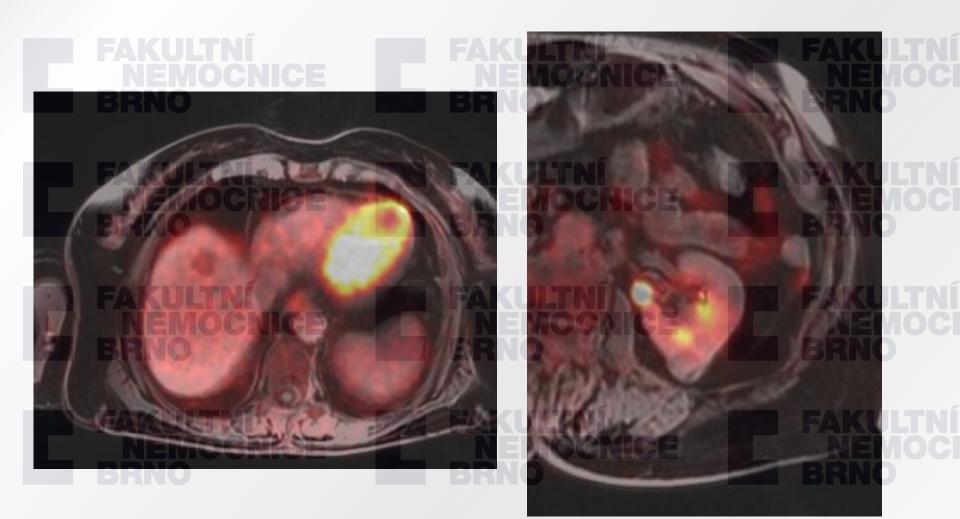
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arteriální f. portovenózní f. hepatospecifická f.







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## Závěr

- < 3 cm metastazování raritní</li>
- metastázy sú většinou s hypervaskularizací
- nefrektomie signál pro hledání metastáz až 30let
- Pozornost žebra, pankreas, měkké tkáně
- uzliny v mediastinu
- hodnocení léčebné odpovědi
- RECIST



