

Detecting liver metastases of melanoma malignum with MRI and immunohistochemistry novel approach in the screening strategy



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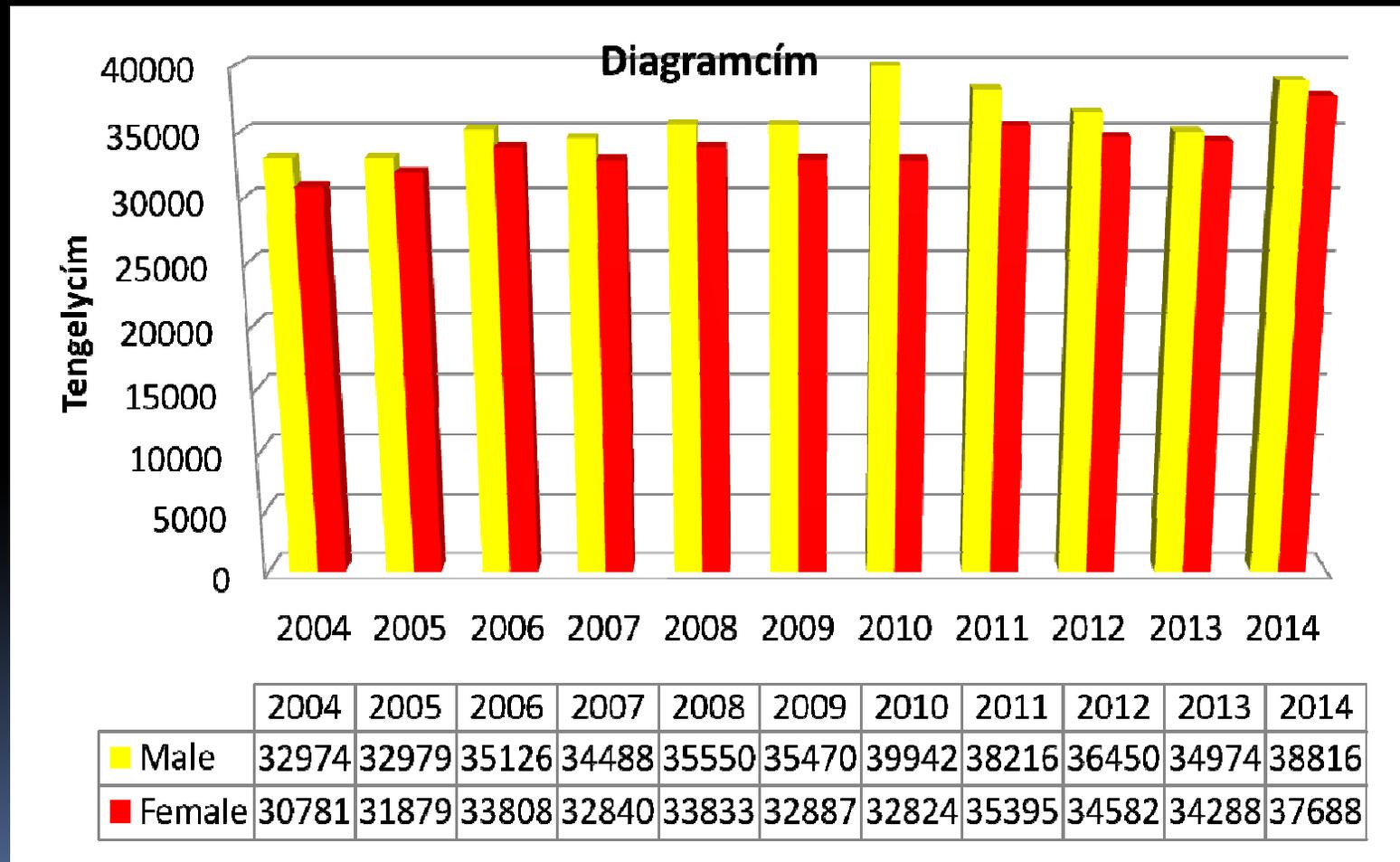
Melanoma malignum becomes more frequent

In the last few decades there are 4 times more male and 3 times more female melanoma patients

Yearly 2000-2500 new patients are registered and approx. 600-700 patients are treated in the National Institute of Oncology

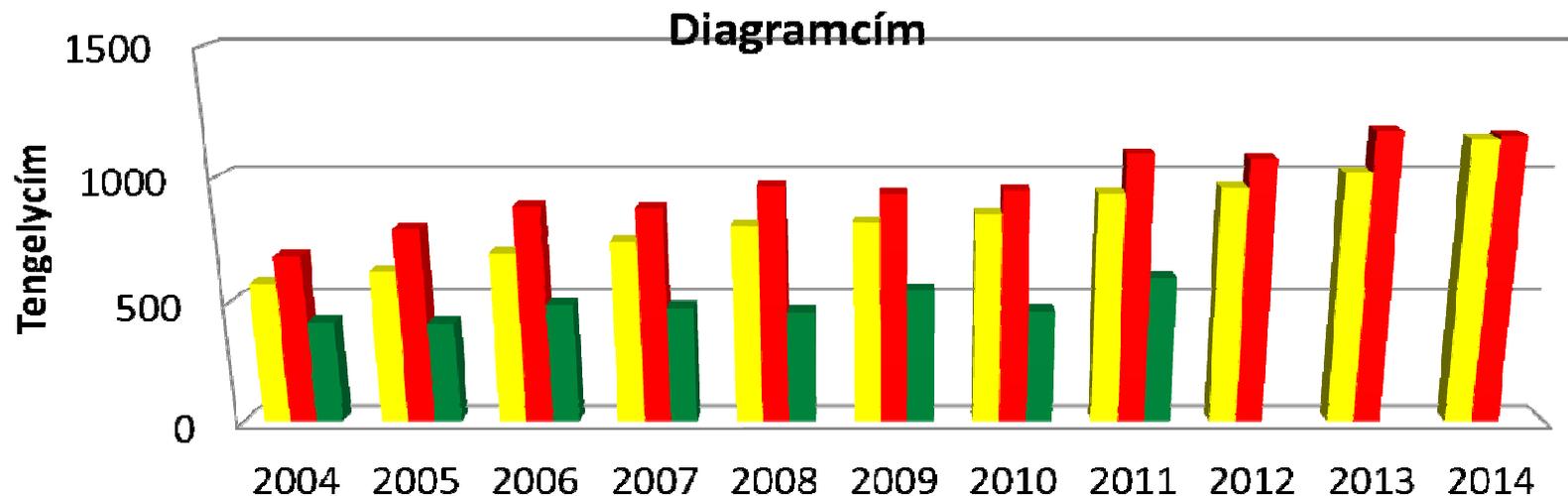
New tumor patients registered in Hungary

(Hungarian Cancer Registry)



New MM patients registered in Hungary

(Hungarian Cancer Registry)



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Male	568	616	692	740	801	813	850	931	953	1011	1142
Female	680	788	879	871	960	930	944	1085	1065	1174	1156
Treated by National Institute of Oncology	410	405	482	471	452	541	457	591	623	657	684

Types of Melanoma malignum

- cutan, ocular and mucosal
- Melanoma >90% on the skin,
most frequent localization:
 - lower extremity(woman)
 - skin on the back(men)

it can start from areas protected against the light,
which indicates the complexe, indirect role of
sunshine.

start from the lymph node and the soft tissue
mucosal melanoma: nasal cavities, sinuses, rectum,

Melanoma Malignum liver MRI findings

Soliter / multiplex laesions

Melanin content - native T1- high signal intensity than its surroundings

large laesions have an inhomogeneous structure

Rarely cystic (<5 %)

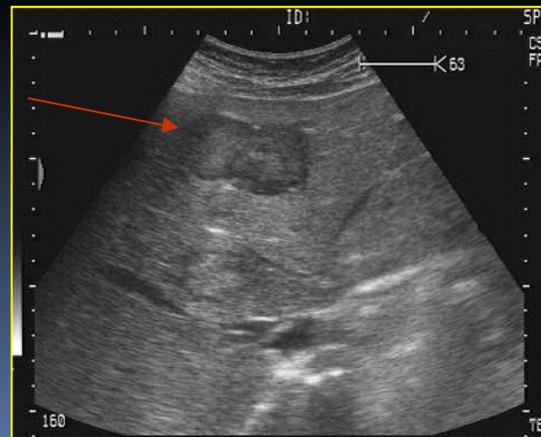
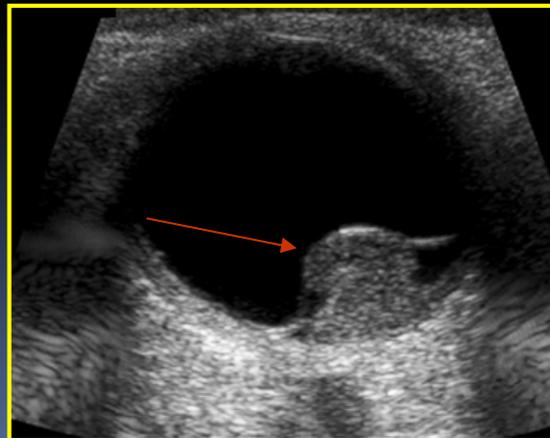
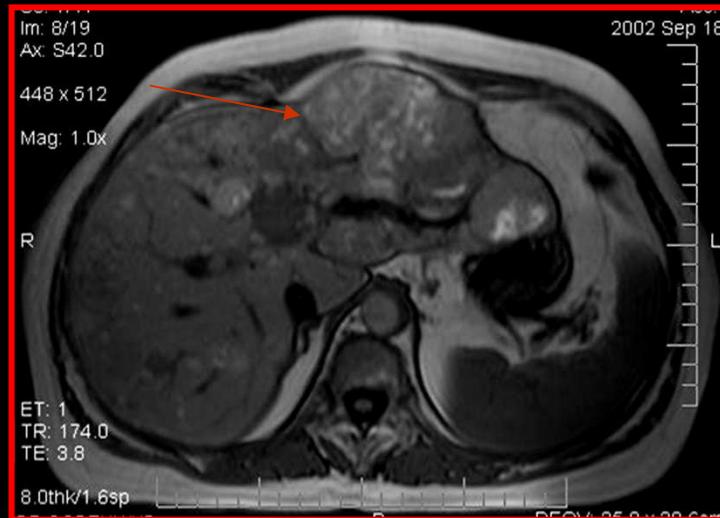
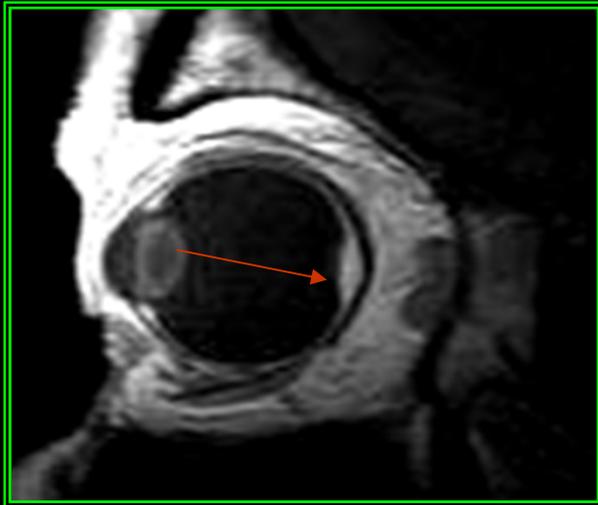
>50% arterial phase contrast enhancement

Ocular melanoma malignant

Second most frequent localization of MM (literature:1-5%)

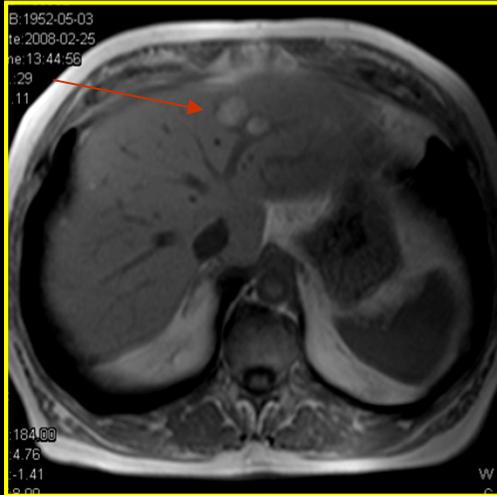
First predilected location: liver

ocular MM: primary tumor, liver& bone metastasrs MRI, T1w

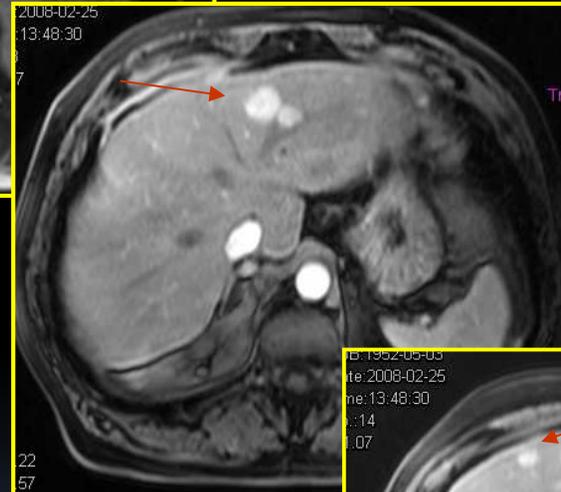
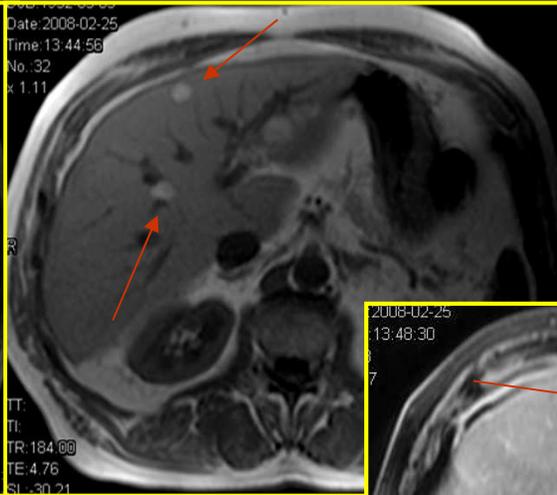


Magnetic Resonance Screening Trial for Hepatic Metastasis in Patients with Locally Controlled Choroidal Melanoma
Tetsuo Maeda, Ukihide Tateishi, Shigenobu Suzuki, Yasuaki Arai, E. Edmund Kim, and Kazuro Sugimura, Division of Diagnostic Radiology and Division of Ophthalmology, National Cancer Center Hospital, Tokyo, Japan,
Division of Diagnostic Imaging, University of Texas, MD Anderson Cancer Center, Houston, TX, USA and Department of Radiology, Kobe University Graduate School of Medicine, Kobe, Japan
Chang AE, Hynds Karnell L, Menck HR. The national cancer database report on cutaneous and noncutaneous melanoma: a summary of 84,836 cases from the last decade. *Cancer*. 1998;83:1664-1678.
Bedikian AY, Legha SS, Mavilgit G, Garracco CH, Khorana S, Piggot G et al. Treatment of uveal melanoma metastatic to the liver: a review of the M.D. Anderson Center experience and prognostic factors. *Cancer*. 1999;76:3655-7.
Uveal Melanoma: Correlation of Histopathologic and Radiologic Findings by Using Thin-Section MR Imaging with a Surface Coil. Arne-Jo'rn Lemke, MD Norbert Hosten, MD Nikolaos E. Bechrakis, MD Andreas Schu'ler, MD Miriam Richter, MD Christian Stroszczynski, MD Roland Felix, MD
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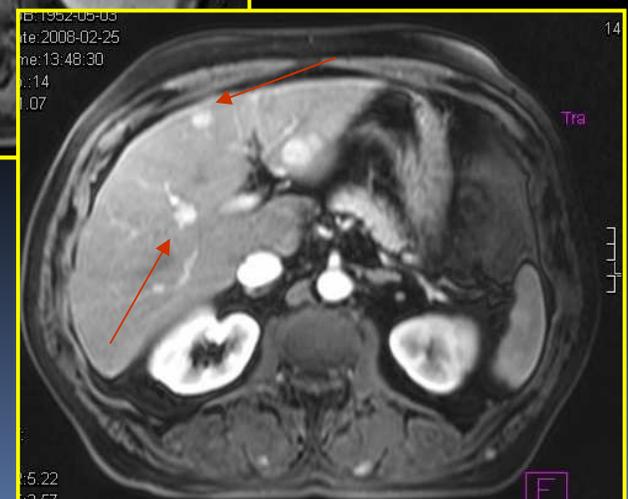
Typical MM liver metastases



T1-weighted
sequences: high
signal intensity



Early
arterial
contrast
enhancing



2004-2014: the examinations

189 liver MRI in case of ocular melanoma patients using extracellular, hepatocytaspecific contrast medium (Gadovist, multihance), and sometimes with RES-specific contrast medium (Resovist, Endorem) (Siemens Symphony 1.5T MR)

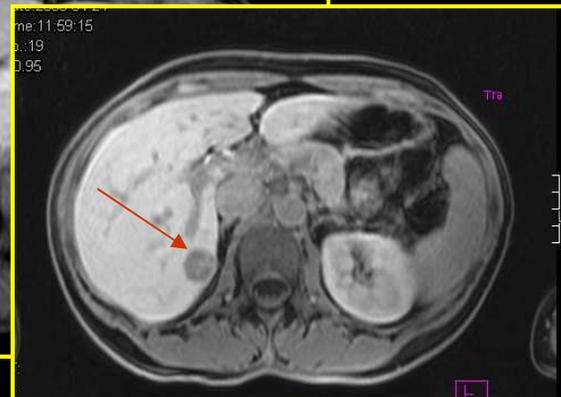
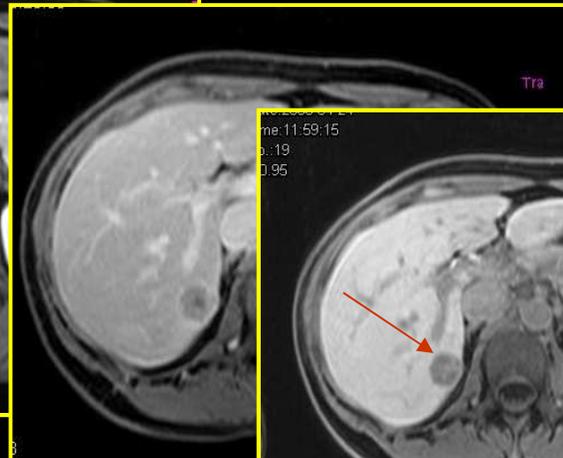
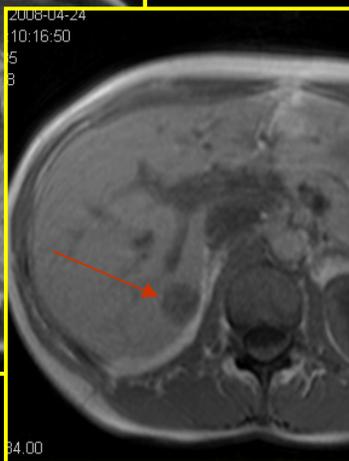
- staging - new patients
- follow-up (3-6 months, according to protocols)
or, in case of patients participating in pharmaceutical studies, according to the clinical protocol

59 patients

- CORE biopsy+liver MRI
- staging or patient follow-up was open to question.
we have evaluated:
 - contrast medium signal intensity (native and contrast medium sequences)
 - compared the results to the histology
 - Additional we investigated various glycosphynogolipid-based tumor associated antigens (GD3 gangliosids and GD3 derivates)

Extracellular, hepatocytoma specific and RES specific contrast media

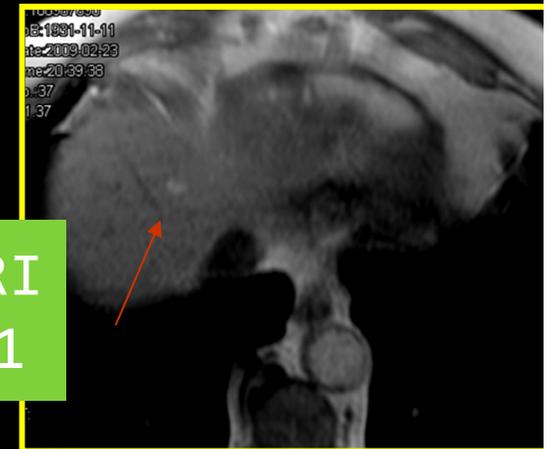
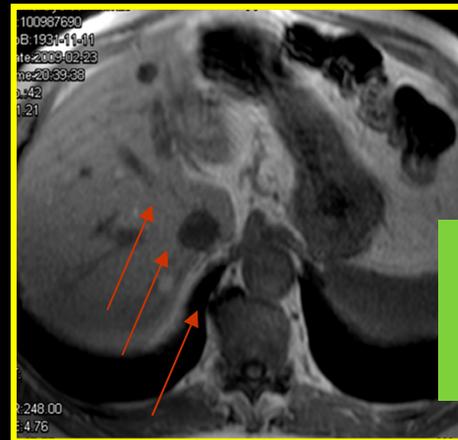
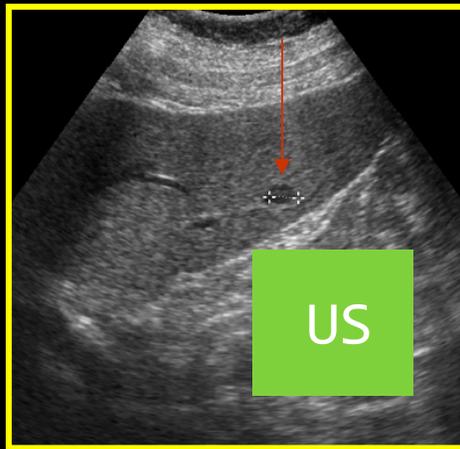
RES specific contrast media



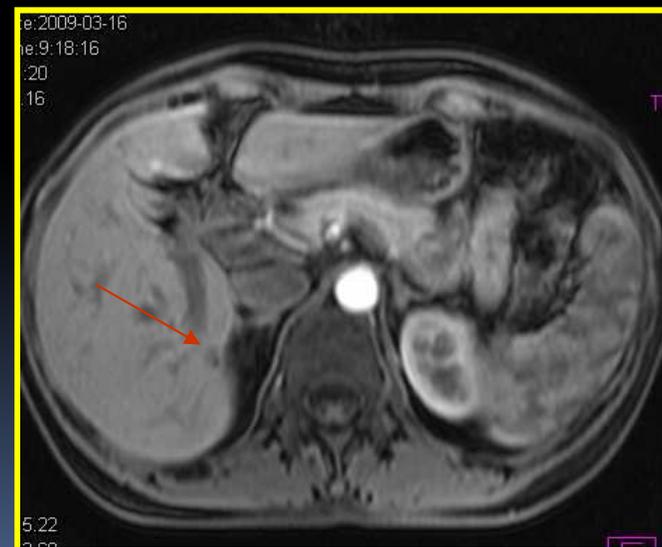
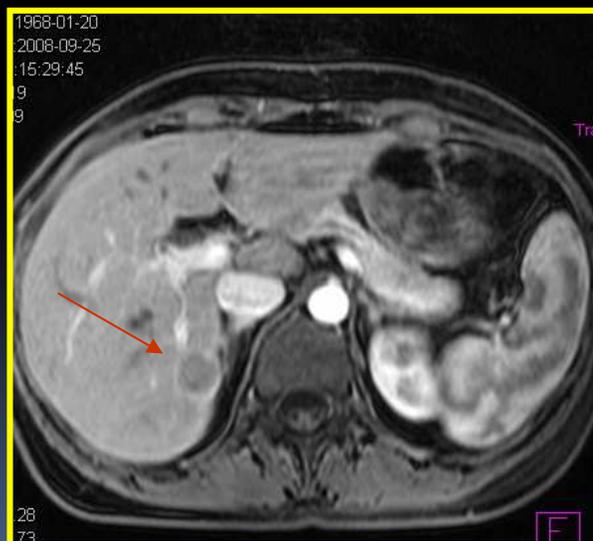
Hepatocytoma-specific

RES-specific

I. Simultan tumors: colon carcinoma& ocular MM

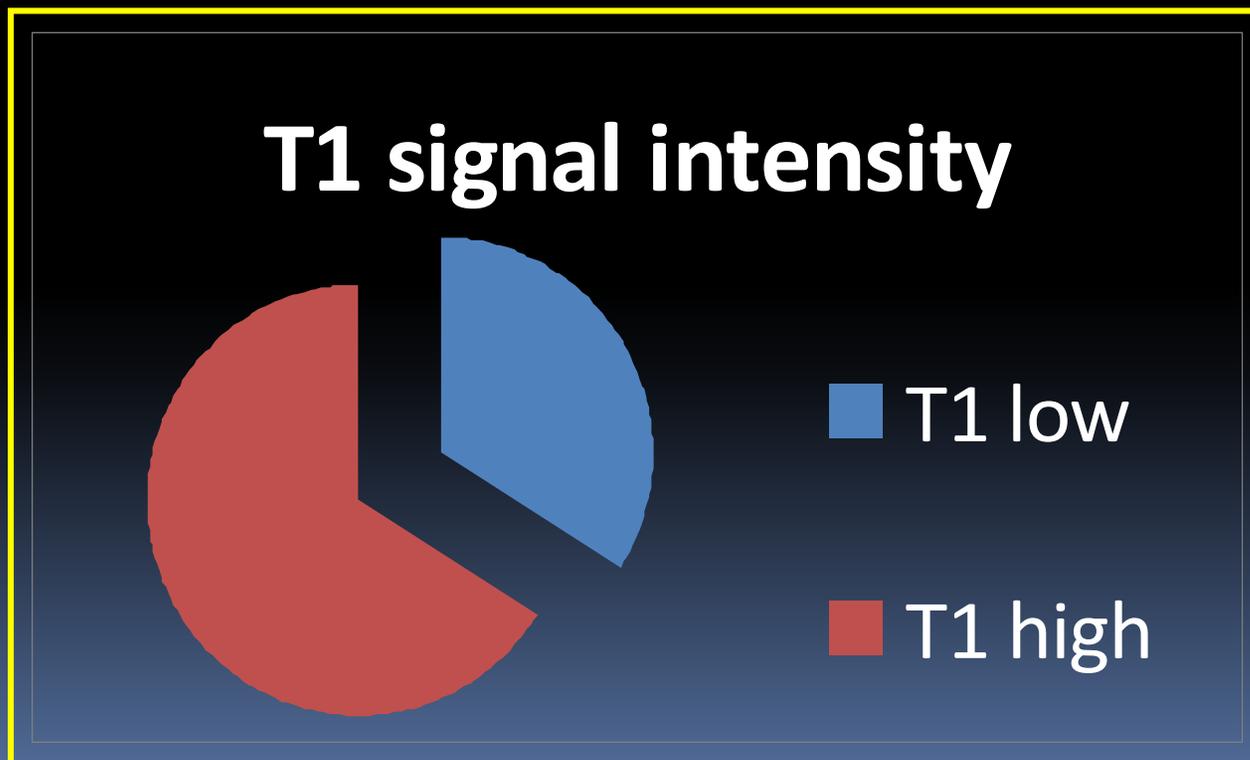


II. Chemotherapy



Signal intensity (native T1 sequences)

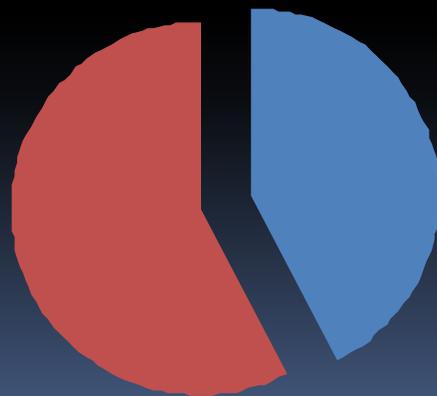
- 39/59 (67%) high signal intensity
- 20/59 (33%) low signal intensity



Contrast dynamics

- 34/59 (58%) **hypervascularisation**
- 26/59 (42%) **hypovascularisation**

Contrast enhancing



■ hypovasc

■ hypervasc

Results

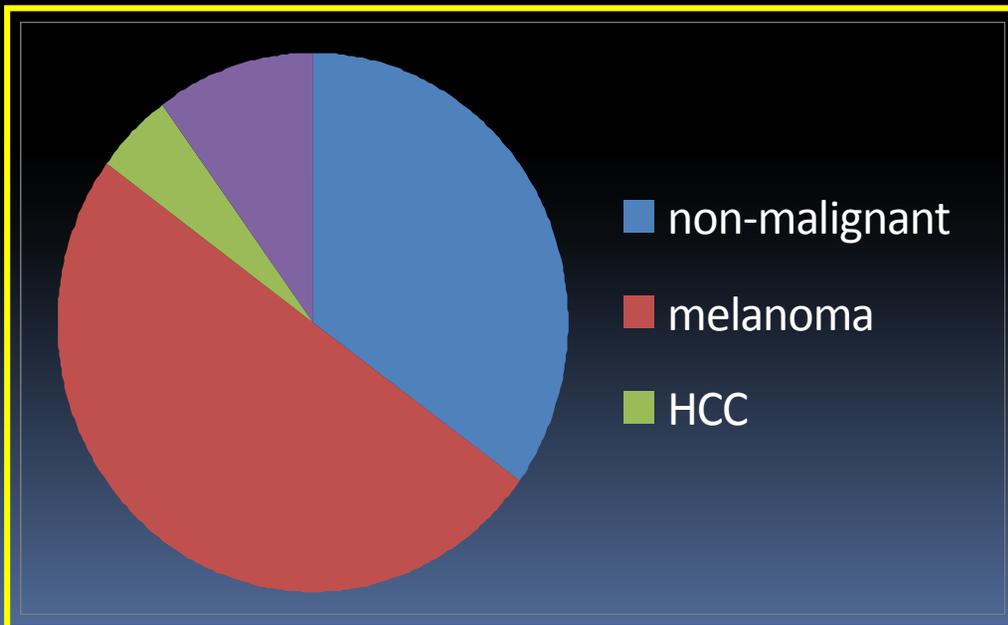
T1 high signal intensity:

confirmed MM metastasis(39/39)

T1 without high signal intensity (20)

- 10 MM
- 1 HCC
- 7 benign laesion
- 2 parabiopsy

the repeated examination confirmed malignity.



Native T1W sequences
without high signal
intensity group

MM liver metastases: immunohistochemistry examination to analyse CORE biopsies

Aim: useful info for further parameters of the formation of metastasis

we analysed:

- cell-type of the malign samples,
- pigmentation
- environmental reactions
- Determining KI67, HMB45, MelanA

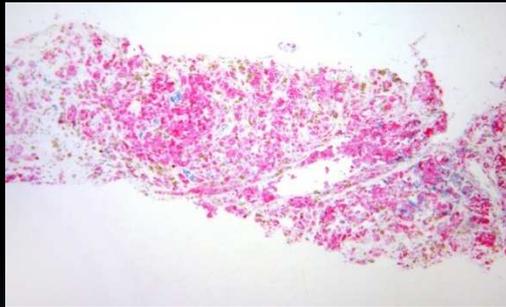
No.	cell type	pigment	HMB45	MeLanA	KI67
n = 5	small cell	0 - 3+	0- 3+	0 - 3+	15% - 80%
n = 18	epitheloid	0 - 3+	0- 3+ (n=16)	0 - 3+ (n=13)	5% - 90%
n = 2	plasmocytoid	0	0 - 1	2 - 3	30% - 40%
n = 3	Spindled cell	1 - 3+	2 - 3+	2 - 3+	10% - 25%
n = 2	histiocytoid	2 - 3+	2+	1 - 3+	50%

Results

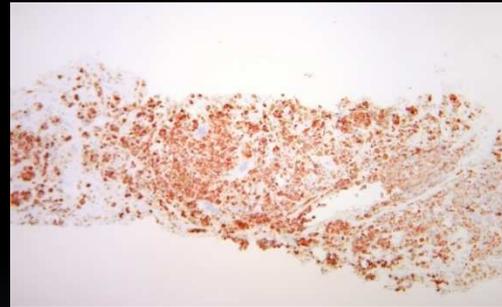
epitheloid character: strong (3+ positive) HMB45 and MelanA signaling extent of proliferation: higher diversity strong signaling

from of tumor proliferation and metastasis formation point of view, it plays an increasingly important role to

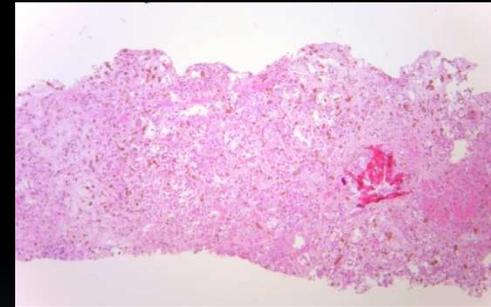
- detect sialylated glycosphingolipids
- make comparative analyses with conventional markers
- detect parallel positive reactions



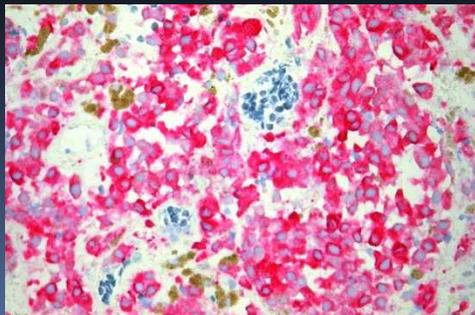
T32 MelanA , Fuchsin, 70x



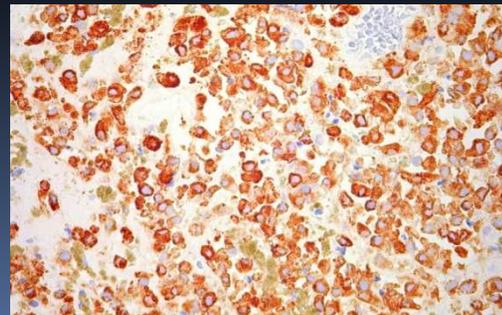
T32 HMB 45, DAB, 70x



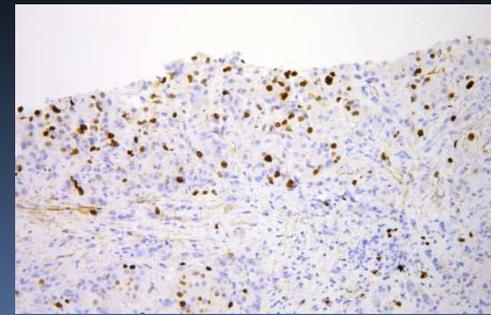
T Haematoxylin - Eosin 100x



T32 MelanA , Fuchsin, 100x



T32 HMB 45, DAB, 100x



T Ki67 proliferacion AG 70x

Lessons and Take Home Messages

In case of high signal intensity on the native T1 sequence, MRI provides a highly reliable diagnosis of metastases containing melanin. It can be detected **without biopsy**, in a **non-invasive** way also

-References show 1-5% of the occurrence of amelanotic melanoma, our examinations showed **>5%**

-Vasularisation of MM metastases vary, showing **high variance**

-Laesions which are less enhancing, present a differencialdiagnostic problem. In these cases **contrast dynamics**, applying **hepatocytta-specific phase** and **follow-up** can provide important additional info

The following factors mean a differencialdiagnostic problem:

- **post-biopsy hemorrhage**
- **bruising** after biopsy
- **lesion** containing **fat (HCC)**

Other clinical factors also have to be taken into consideration



Thank you very much for your attention!

Melanoma epidemiology and trends Germany Clinics in Dermatology(2009) 27, 3–9 Claus Garbe, MD, Ulrike Leiter L, Menck HR.

Hungarian cancer registry 2014 Forrás: Rákregiszter&OII

The national cancer database report on cutaneous and noncutaneous melanoma: a summary of 84,836 cases from the last decade, *Cancer*. 1664-1678 &

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³Division of Diagnostic Imaging, University of Texas, MD Anderson Cancer Center, Houston, TX, USA and⁴Department of Radiology, Kobe University Graduate School of Medicine, Kobe, Japan

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The Stage of Melanogenesis in Amelanotic Melanoma

Naoki Oiso and Akira Kawada *Department of Dermatology, Kinki University Faculty of Medicine Japan*

Comparative study of two whole-body imaging techniques in the case of melanoma metastases: Advantages of multi-contrast MRI examination including a diffusion-weighted sequence in comparison with PET-CT

Valérie Laurent^{a,*}, Grégory Trausch^b, Olivier Bruot^a, Pierre Olivier^c, Jacques Felblinger^d, Denis Régenta

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Detectability of liver metastases in malignant melanoma: prospective comparison of magnetic resonance imaging and positron emission tomography

Nadir Ghanema^{*}, Carsten Althoefer^a, Stefan Högerleb^a, Egbert Nitzsche^b,

Christian Lohmann^a, Oliver Schäfer^a, Elmar Kottera^a, Mathias Langer^a

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MR imaging of hepatic metastasis in patients with malignant melanoma: Evaluation of suspected lesions screened at contrast-enhanced

CT Keitaro Sofue^{a,*}, Ukihide Tateishi^a, Masakatsu Tsurusakia, Yasuaki Arai^a, Naoya Yamazaki^b, Kazuro Sugimura^c

Staging of cutaneous melanoma P. Mohr^{1*}, A. M. M. Eggermont², A. Hauschild³ & A. Buzaid⁴

Annals of Oncology 20 (Supplement 6): vi14–vi21, 2009 doi:10.1093/annonc/mdp256

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