

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



Gyorgy Naszados¹, Beatrix Kotlan^{2,3}, Vanda Plotar², Szabolcs Horvath², Klara Eles², Erika Toth², Gabriella Liszkay^{4,6}, Miklos Kasler^{5,6} and Maria Godeny^{1,6}

¹Department of Diagnostic Radiology, National Institute of Oncology, Budapest, Hungary

²Center of Surgical and Molecular Tumorpathology, National Institute of Oncology, Budapest, Hungary

³Molecular Immunology and Toxicology, National Institute of Oncology, Budapest, Hungary

⁴Department of Oncodermatology, National Institute of Oncology, Budapest, Hungary

⁵Board of Directors, National Institute of Oncology, Budapest, Hungary

⁶Department of Postgraduate Education and Scientific Research of the University of Medicine and Pharmacy Tingu Mures

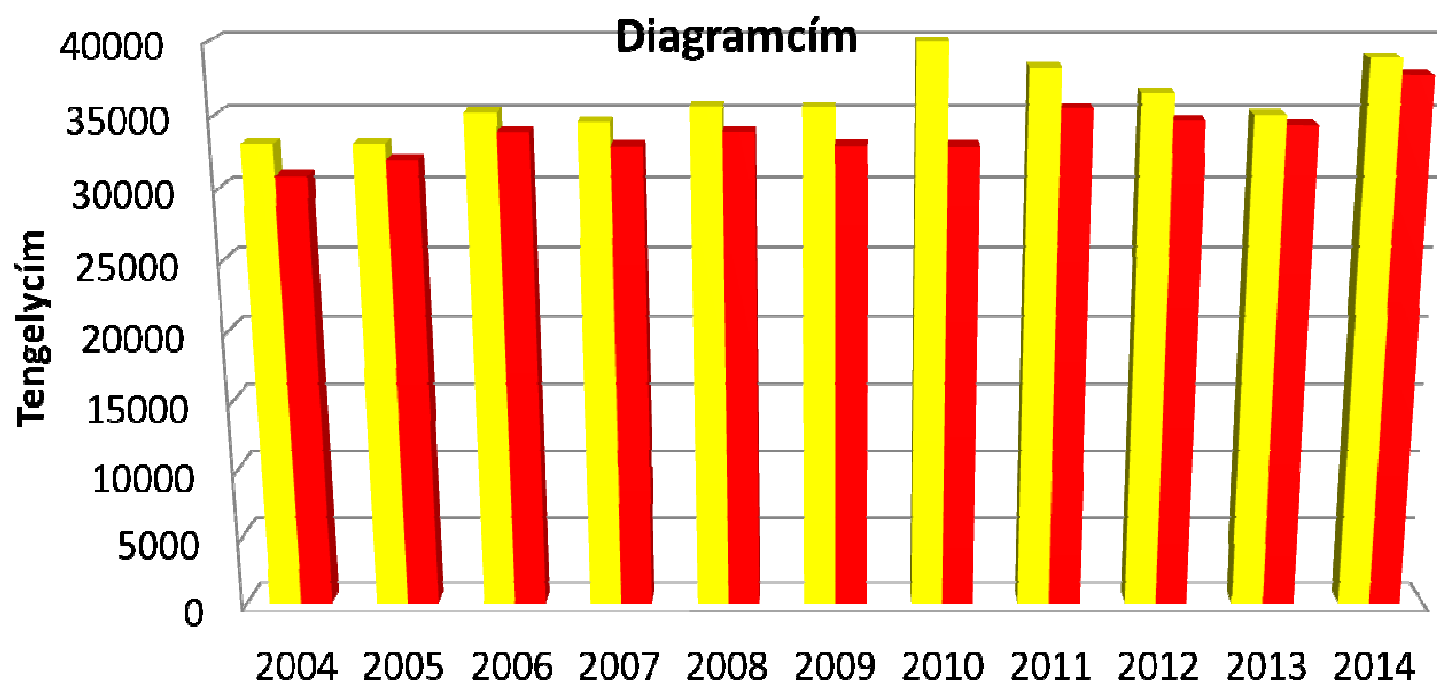
Melanoma malignum becomes more frequent

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

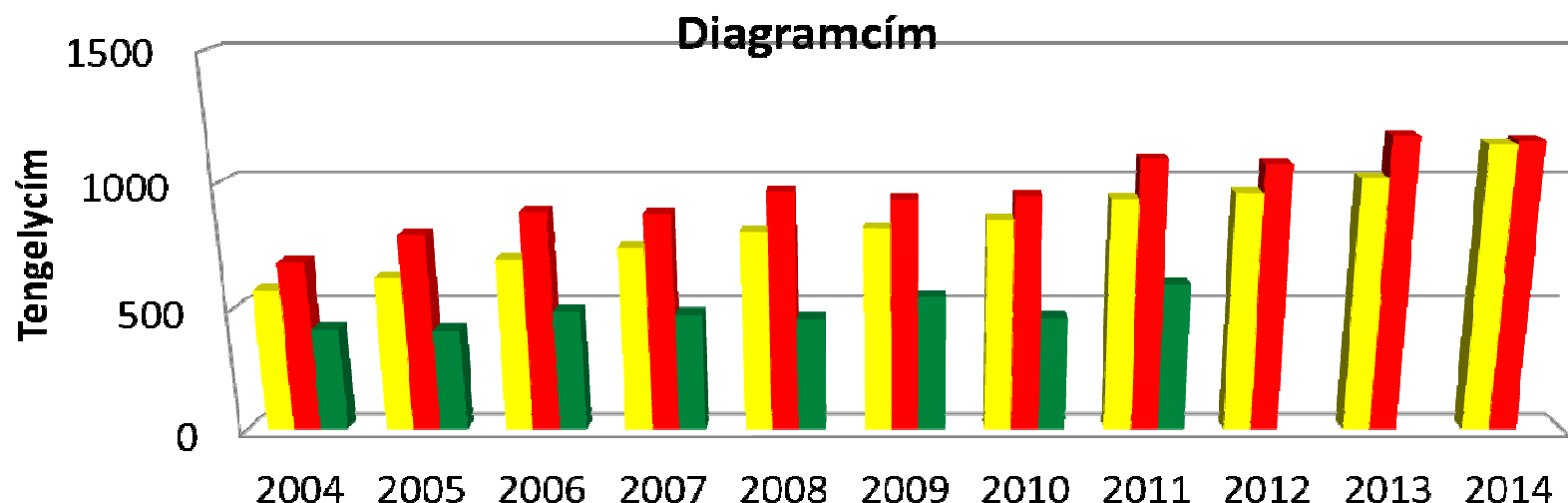
(Hungarian Cancer Registry)



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Male	32974	32979	35126	34488	35550	35470	39942	38216	36450	34974	38816
Female	30781	31879	33808	32840	33833	32887	32824	35395	34582	34288	37688

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 %)

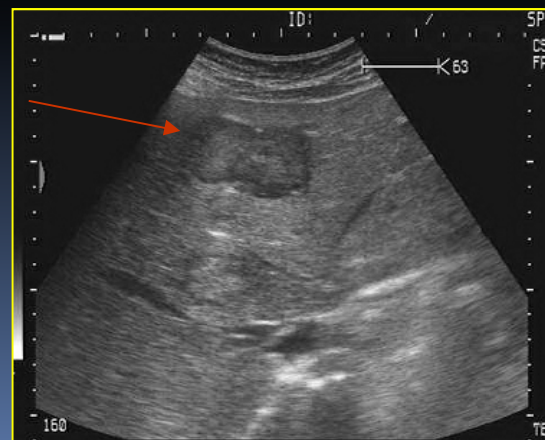
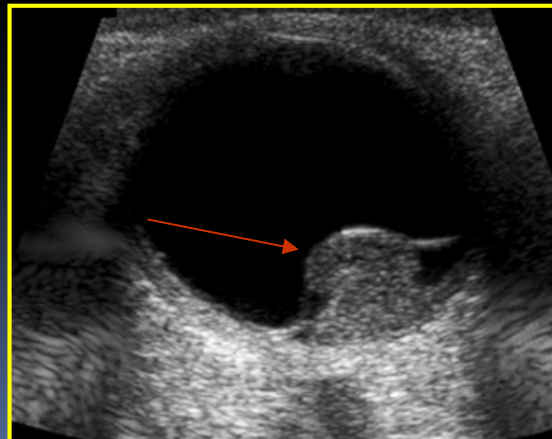
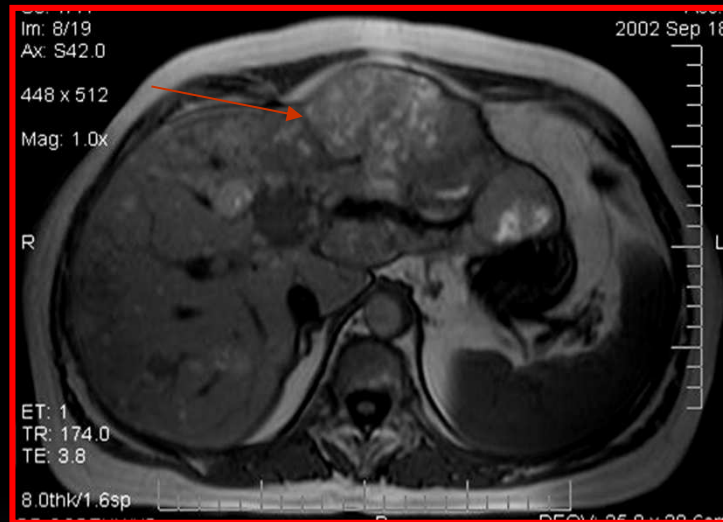
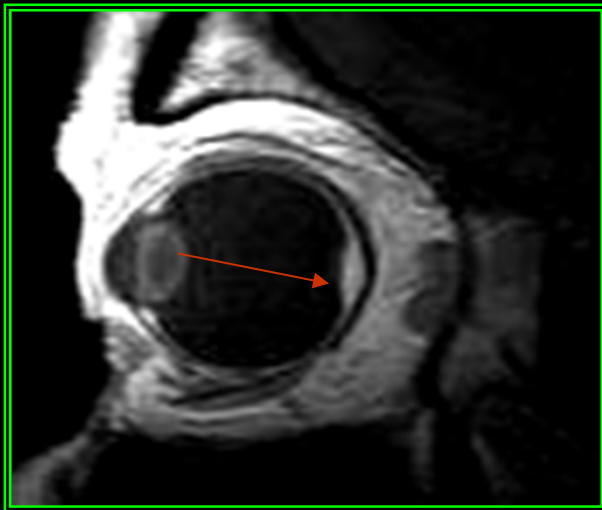
>50% arterial phase contrast enhancement

Ocular melanoma malignant

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

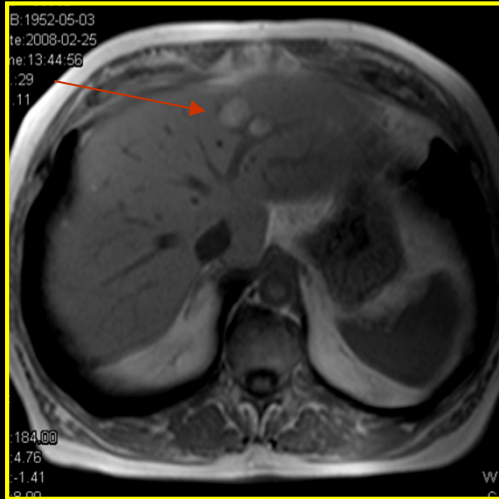
First predilected location: liver

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

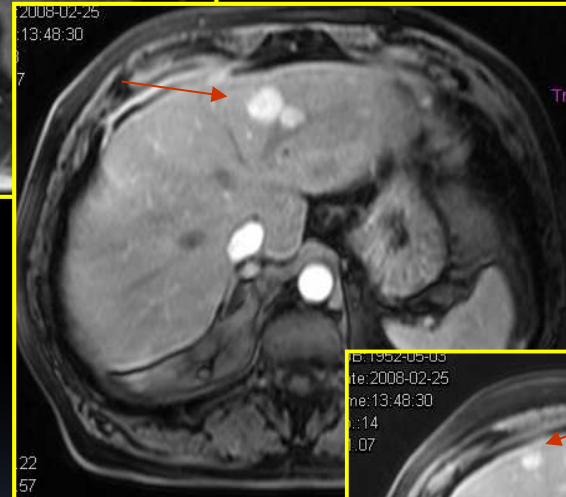
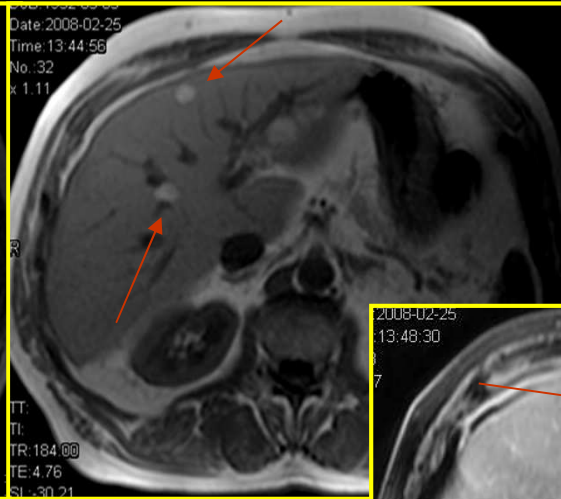


Magnetic Resonance Screening Trial for Hepatic Metastasis in Patients with Locally Controlled Choroidal Melanoma
Tetsuo Maeda, Ukihide Tateishi, Shigenobu Suzuki, Yasuaki Arai, E. Edmund Kim and Kazuo Sugimura^{1,2} Division of Diagnostic Radiology and ³Division of Ophthalmology, National Cancer Center Hospital, Tokyo, Japan,
³Division of Diagnostic Imaging, University of Texas, MD Anderson Cancer Center, Houston, TX, USA and ⁴Department of Radiology, Kobe University Graduate School of Medicine, Kobe, Japan
Chang AE, Hynds Karmell 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, Mavilgiti G, Carrasco CH, Khorana S, Plager G, et al. Treatment of uveal melanoma metastatic to the liver: a review of the M.D. Anderson Center experience and prognostic factors. *Cancer*. 1995;76:1665-7.
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 Norbert Bornfeld, MD Nikolaos E. Bechrakis, MD Andreas Schu'ler, MD Miriam Richter, MD Christian Stroszczynski, MD Roland Felix, MD
MR imaging of primary choroidal melanoma P.B. Hanagandi, F. G. Gonçalves, C. Torres, J. Chankowsky, R. D. C. O'donovan, Montreal, QC/CA

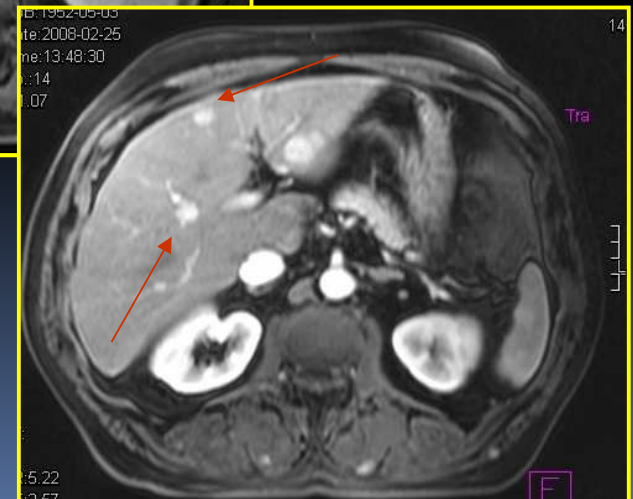
Typical MM liver metastases



T1-weighted
sequences: high
signal intensity



Early
arterial
contrast
enhancing



2004-2014: the examinations

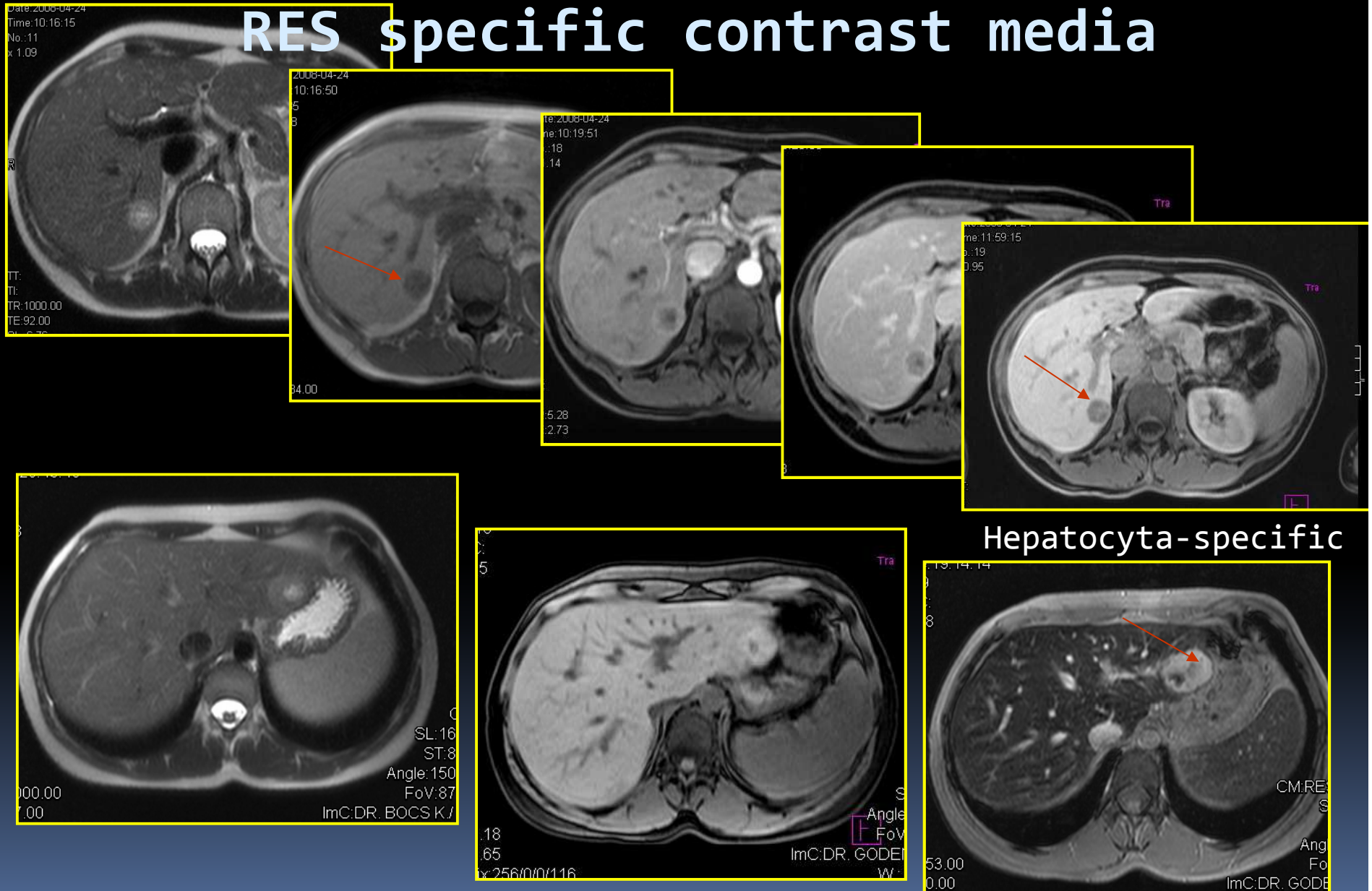
189 liver MRI in case of ocular melanoma patients using extracellular, hepatocytaspecific contrast medium (Gadovist, multihance), and sometimes with RES-specific contrast medium (Resovist, Endorem) (Siemens Symphony 1.5T MR)

- 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)

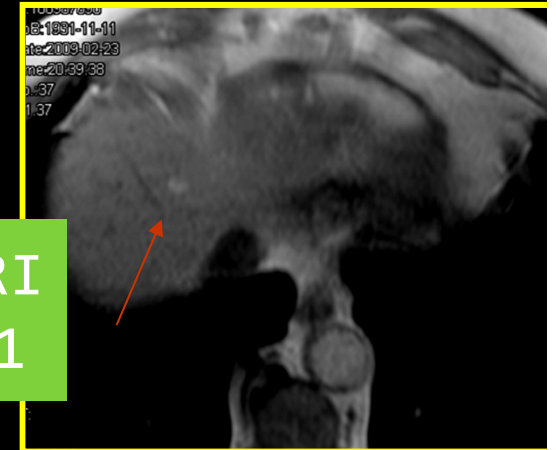
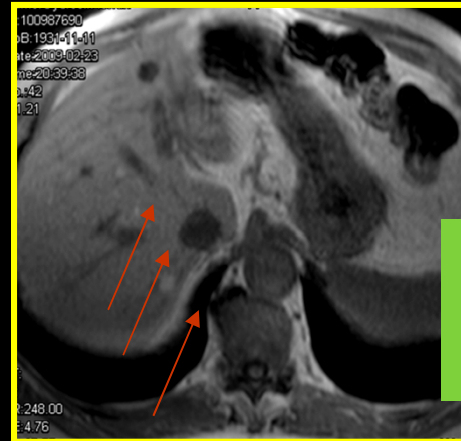
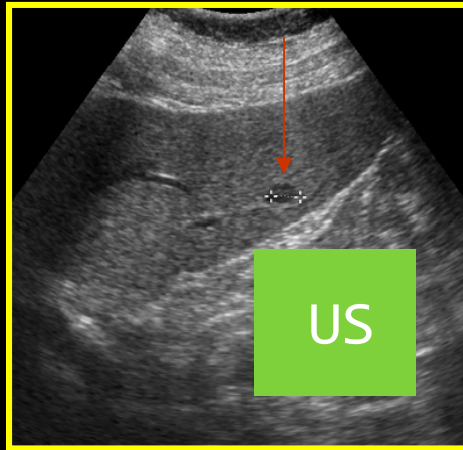
Extracellular, hepatocytaspecific and RES specific contrast media



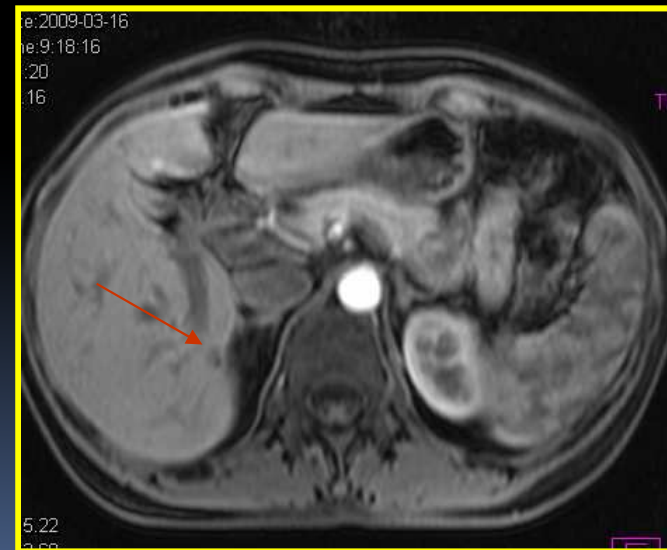
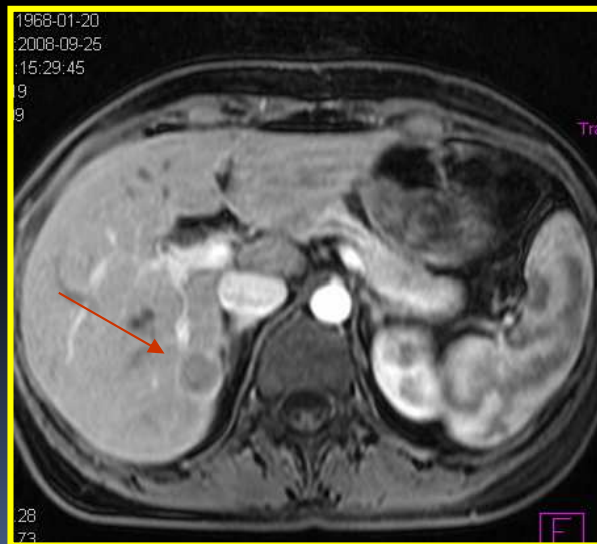
Hepatocytaspecific

RES-specific

I. Simultan tumors: colon carcinoma& ocular MM

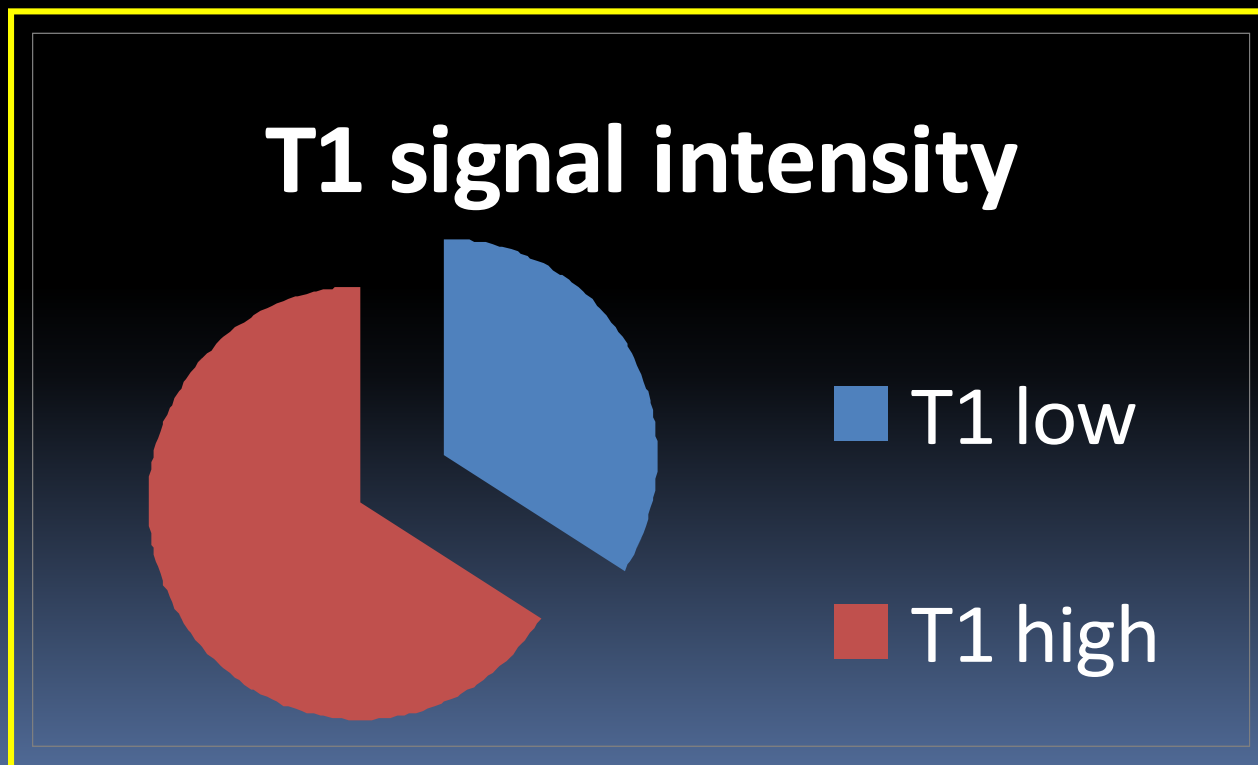


II. Chemotherapy



Signal intensity (native T1 sequences)

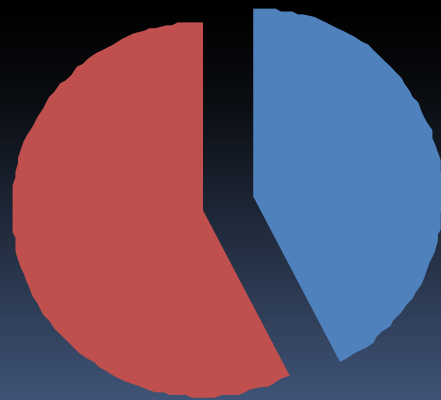
- 39/59 (67%) high signal intensity
- 20/59 (33%) low signal intensity



Contrast dynamics

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

Contrast enhancing



■ hypovasc

■ hypervasc

Results

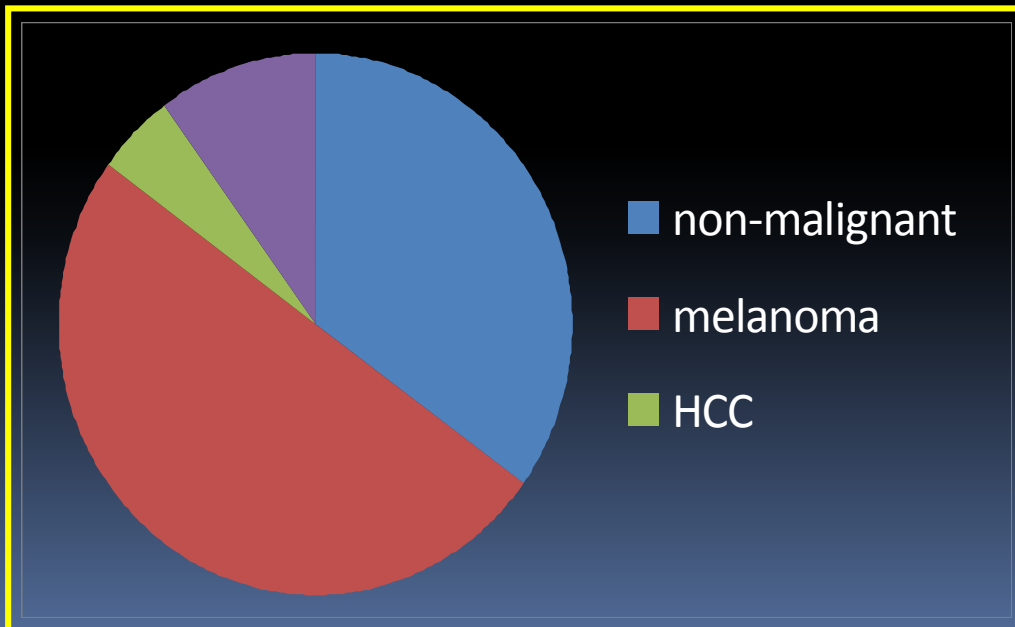
T1 high signal intensity:

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

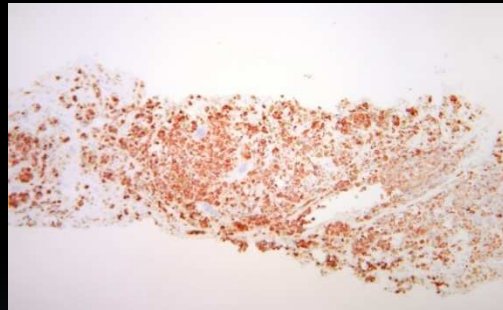
epitheloid character: strong (3+ positive) HMB45 and MelanA signaling extent of proliferation: higher diversity strong signaling

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

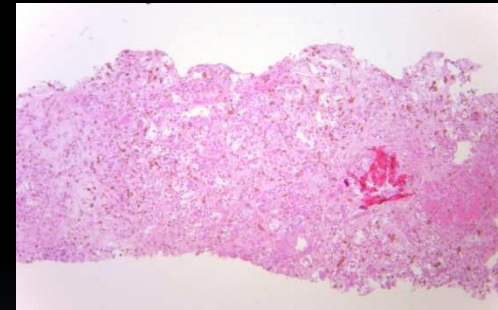
- detect sialylated glycosphingolipids
- make comparative analyses with conventional markers
- detect parallel positive reactions



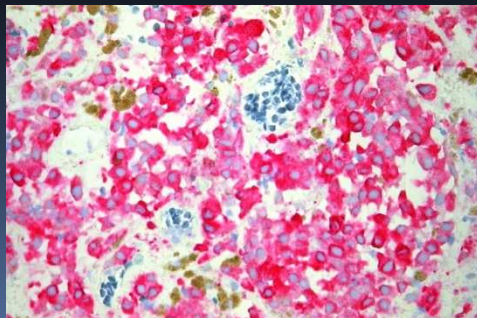
T32 MelanA , Fuchsin, 70x



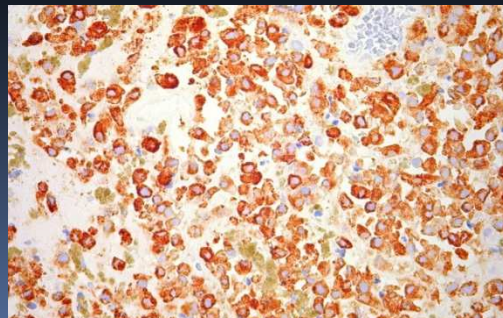
T32 HMB 45, DAB, 70x



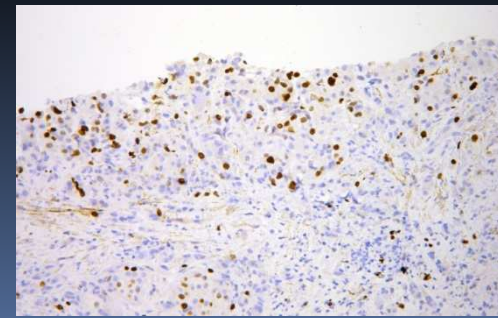
T Haematoxylin - Eosin 100x



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 **hepatocyta-specific phase** and **follow-up** can provide important additional info

The following factors mean a differencialdiagnostic problem:

- **post-biopsy hemorrhage**
- **bruising** after biopsy
- **leasion** 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, MD¹, Ulrike Leiter L, Menck HR.

Hungarian cancer registry 2014 Forrás: Rákregiszter⁸⁰⁰¹

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

Magnetic Resonance Screening Trial for Hepatic Metastasis in Patients with Locally Controlled Choroidal Melanoma

Tetsuo Maeda¹, Ukihide Tateishi¹, Shigenobu Suzuki², Yasuaki Arai¹, E. Edmund Kim³ and Kazuro Sugimura⁴¹Division of Diagnostic Radiology and, ²Division of Ophthalmology, National Cancer Center Hospital, Tokyo, Japan,

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

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, Carrasco CH, Khorana S, Plager C, et al. Treatment of uveal melanoma metastatic to the liver: a review of the M.D. Anderson Center experience and prognostic factors. *Cancer* 1995;76:1665–7

Uveal Melanoma: Correlation of Histopathologic and Radiologic Findings by Using Thin-SectionMR Imaging with a Surface Coil¹

Arne-Jo¹rn Lenke, MD Norbert Hosten, MD Norbert Bornfeld, MD Nikolaos E. Bechrakis, MD Andreas Schu¹ler, MD Miriam Richter, MD Christian Stroszczynski, MD Roland Felix, MD

MR imaging of primary choroidal melanoma P. B. Hanagandi, F. G. Gonçaves, C. Torres, J. Chankowsky, R. D. C. O'donovan; Montreal, QC/CA

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

^a *Department of Adult Radiology, Brabois Hospital, University of Nancy, 54500 Vandoeuvre-Lès-Nancy, France*

^b *GE Healthcare Technologies, 283 rue de La Minière, 78533 Buc CEDEX, France*

^c *Department of Nuclear Medicine, Brabois Hospital, University of Nancy, 54500 Vandoeuvre-Lès-Nancy, France*

^d *IADI Laboratory, INSERM-ERI 13, University of Nancy, 54500 Vandoeuvre-Lès-Nancy, France*

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

Nadir Ghanema^{*,}, Carsten Althoefer^a, Stefan H¹ogerleb, Egbert Nitzsche^b,

Christian Lohmanna, Oliver Sch¹afera, Elmar Kottera, Mathias Langera

^a *Departments of Diagnostic Radiology, University Hospital Freiburg, Freiburg 79106, Germany* ^b *Departments of Nuclear Medicine, University Hospital Freiburg, Freiburg, Germany*

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 Tsurusaki^a, Yasuaki Araia^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

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

Nadir Ghanema^{*,}, Carsten Althoefer^a, Stefan H¹ogerleb, Egbert Nitzsche^b, Christian Lohmanna, Oliver Sch¹afera, Elmar Kottera, Mathias Langera