A knowledge based system for the prediction of metastatic disease in patients with malignant melanoma

DI Christian Scheibböck

Preview

- Skin cancer
  - Malignant melanoma
- Prediction model
- Next steps

DI Christian Scheibböck

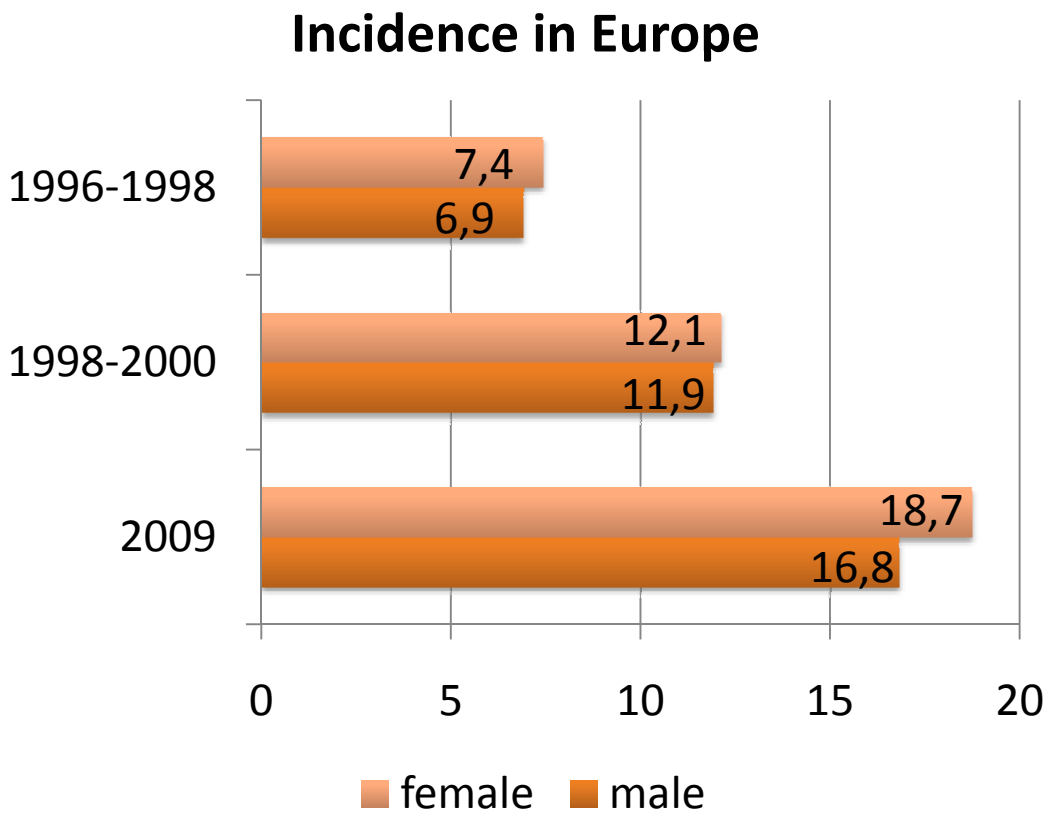
Skin cancer in general

- **Basal cell carcinoma** (metastasis rare)
- **Spindle cell carcinoma** (metastasis rare)
- **Malignant melanoma -** responsible for death about 90% of skin cancer (fast metastasis)

Metastasis is defined as a spreading of tumour cells in distant regions of the body with an additional growth of a further tumour.

DI Christian Scheibböck

Malignant melanoma



DI Christian Scheibböck

Malignant melanoma

Diagnosis

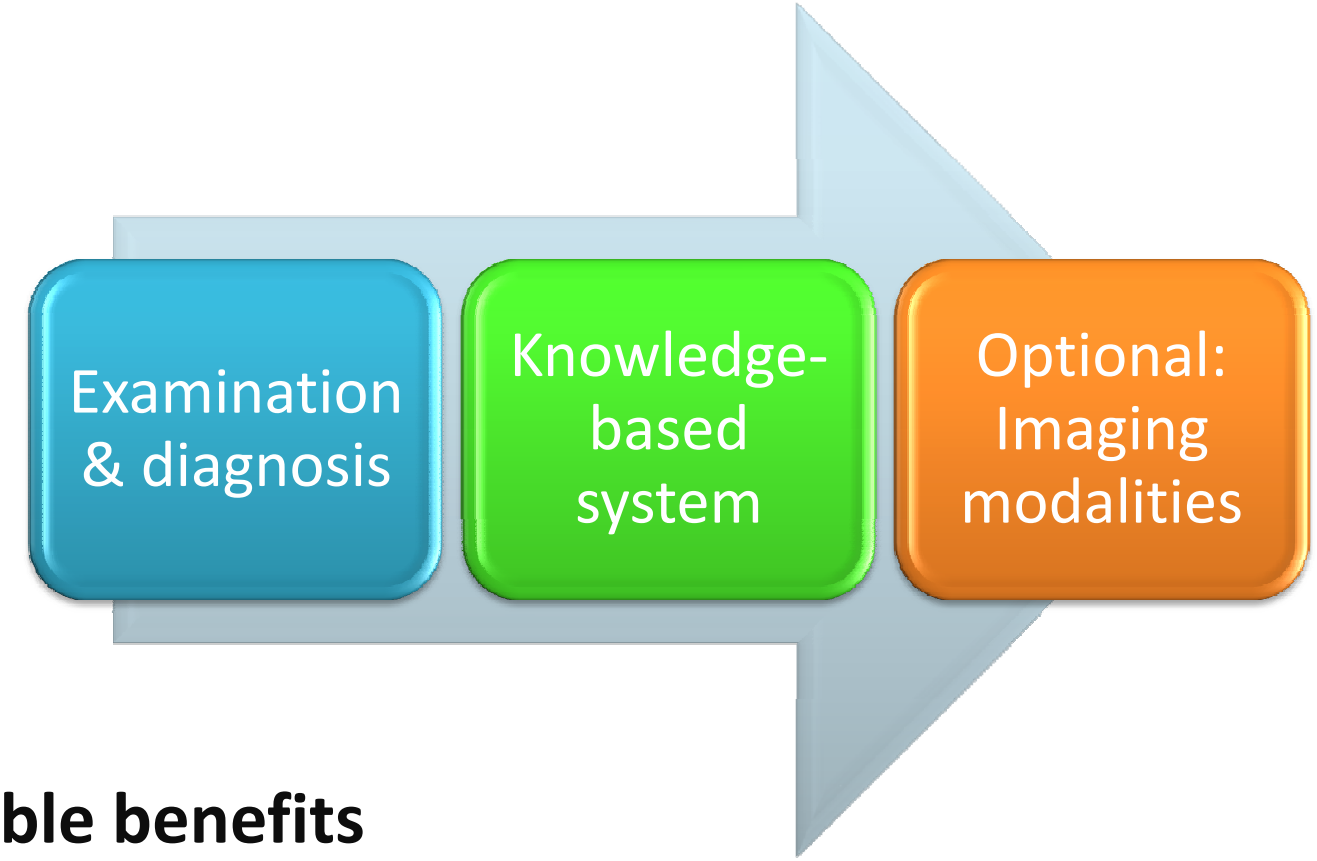
- ABCDE-rule (80% diag. sensitivity)
- Dermoscopy (90% diag. sensitivity)

Follow-up examinations detecting metastasis

- Chest X-ray
- Computed tomography (CT)
- Magnetic resonance tomography (MRT)
- Positron emission tomography (PET)
- Serum parameters – “Tumour markers”

DI Christian Scheibböck

Malignant melanoma



Possible benefits

- Increasing the wellbeing of the patients
- Reduction of stress caused by additional examinations

DI Christian Scheibböck

Prediction model

➔Prediction of metastatic events in patients with melanoma

Knowledge base with combined results (programmed in Arden-Syntax):

1. Interpretation of tumour markers
2. Pre-test probability for metastasis
3. Interpretation of the current probability of metastasis

DI Christian Scheibböck

Interpretation of tumour markers

Tumour markers are circulating macro molecules which will be obtained from blood or other body fluids.

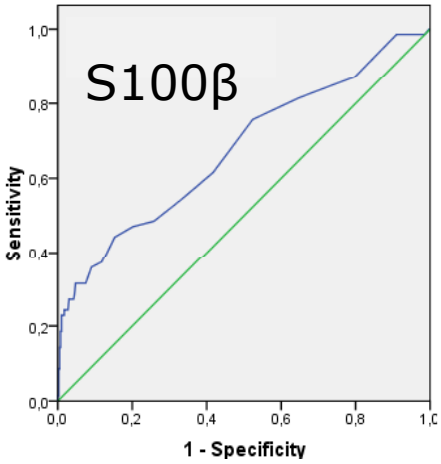
Our Hypothesis

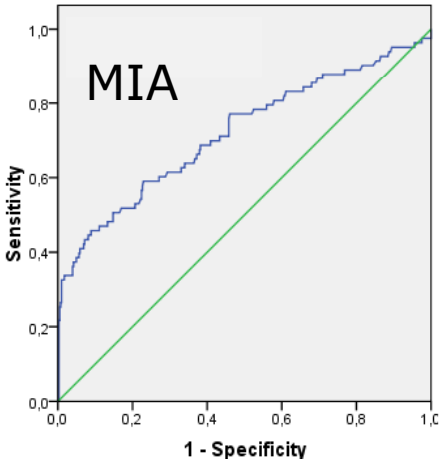
The presence of metastatic disease correlates with the concentration of tumour markers.

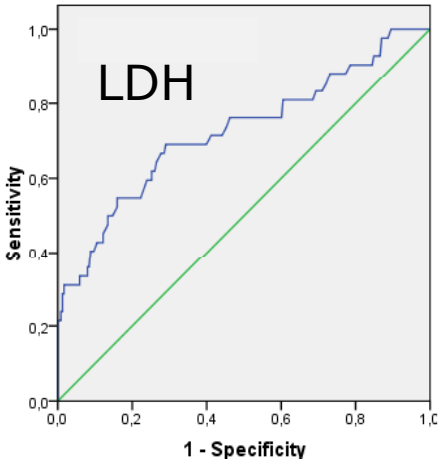
DI Christian Scheibböck

Melanoma tumour markers

S100β, MIA, LDH (493 records)







	median	IQR	min	max	highest sensitivity / specificity
S100β	**0.06**	**0.05**	**0.002**	**7.81**	**61.43% / 58.40%**
MIA	**7.175**	**4.475**	**0.003**	**1023**	**63.86% / 66.09%**
LDH	**175**	**54**	**90**	**2842**	**69.05% / 67.23%**

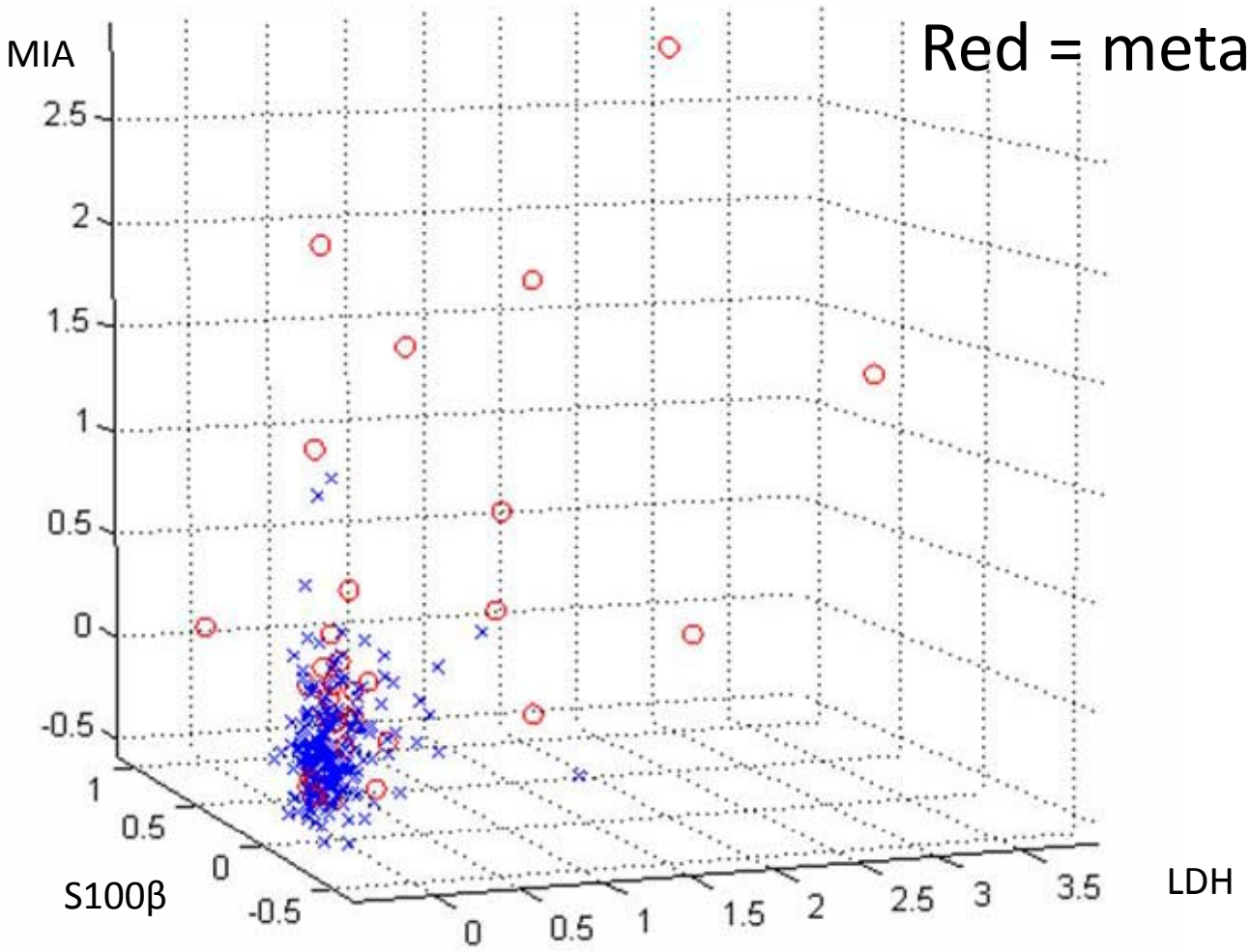
Quelle: **Schlager, Katharina. 2009.** Klinischer Vorhersagewert der Tumormarker S100β, MIA und LDH. [Diplomarbeit]. Wien : s.n., 2009

DI Christian Scheibböck

3D visualization of tumour markers (S100ß, MIA, LDH)

Blue = no metastasis

Red = metastasis



DI Christian Scheibböck

Methods

(1) Multivariate statistical methods

- Logistic regression

(2) Machine Learning

- Artificial neural network (scaled conjugate gradient optimization with 20 hidden neurons)

DI Christian Scheibböck

Interpretation of tumour markers

Results - Logistic regression

	Data set pos/neg	AUC	95% Asymptotic CI	max. sensitivity / specificity	Asymptotic sign.
S100β	469 70 / 399	0.676	0.601 – 0.750	61.40% / 58.40%	<0.0001
MIA	489 83 / 406	0.720	0.651 – 0.790	63.90% / 66.01%	<0.0001
LDH	280 42 / 238	0.724	0.630 – 0.818	69.00% / 71.00%	<0.0001

DI Christian Scheibböck

Interpretation of tumour markers

Results - Artificial neural network

	Data set pos/neg	AUC	95% Asymptotic CI	max. sensitivity / specificity	Asymptotic sign.
S100β	469 70 / 399	0.676	0.601 – 0.750	54.30% / 66.90%	<0.0001
MIA	489 83 / 406	0.720	0.651 – 0.790	63.90% / 66.01%	<0.0001
LDH	280 42 / 238	0.724	0.630 – 0.818	69.00% / 71.01%	<0.0001

Combined parameters	Data set pos/neg	AUC	95% Asymptotic CI	max. sensitivity / specificity	Asymptotic sign.
S100β/MIA/LDH incl. MV	493 85 / 408	0.739	0.673 – 0.805	67.10% / 69.12%	<0.0001
S100β/MIA/LDH	270 37 / 233	0.734	0.631 – 0.837	73.00% / 68.67%	<0.0001

DI Christian Scheibböck

Pre-test probability

The estimation of pre-test probability is of utmost importance for accurate clinical reasoning.[1]

Already *Thomas Bayes* engaged oneself with the pre-test probability of events.[2]

[1]http://www.merck.com/mmpe/sec22/ch328/ch328e.html
[2]http://en.wikipedia.org/wiki/Thomas_Bayes

DI Christian Scheibböck

Pre-test probability

Calculation of the probability for metastasis and tumour stage classification (TNM-classification):

- **T**umour (Tumour thickness, Ulceration, Mitosis)
- **N**odes (Number of the nodes)
- **M**etastasis (Localization of the metastasis)

DI Christian Scheibböck

Current probability of survival

Original hazard model

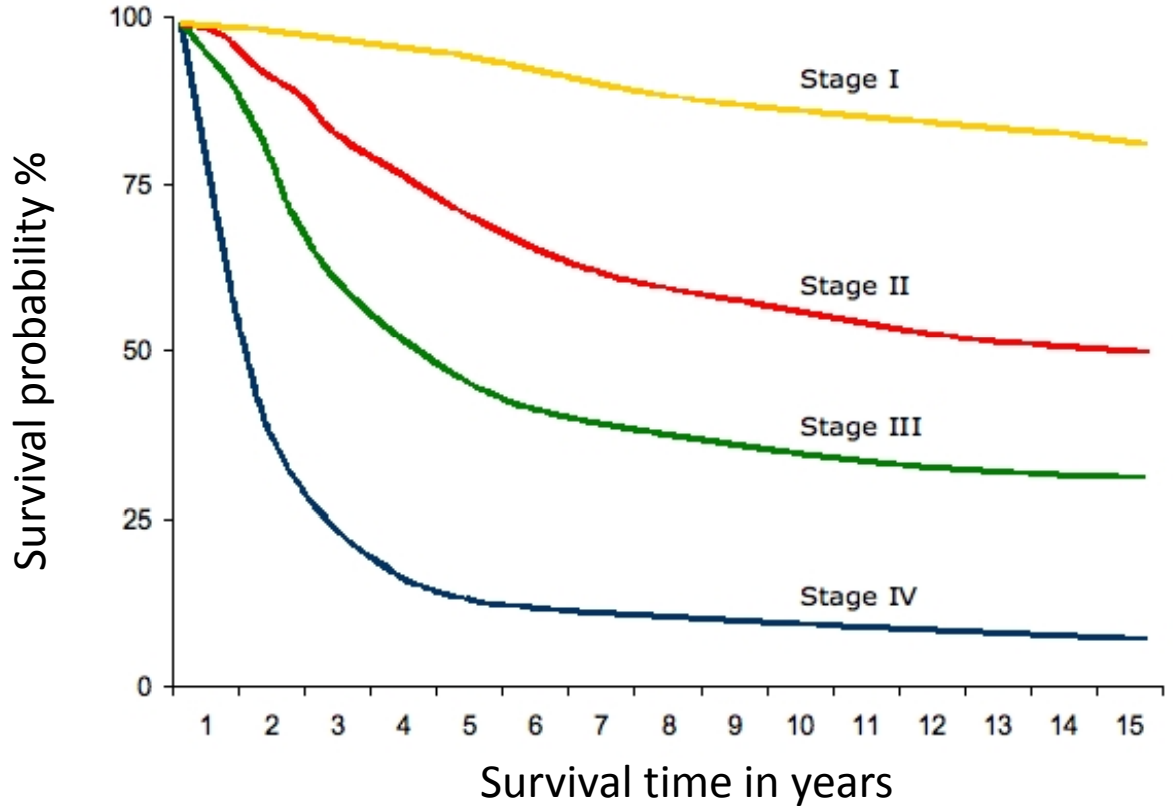
$$h(x) = \lambda e^{\beta x}$$

$$h'(x) = \lambda \beta e^{\beta x}$$

Enhanced hazard model

$$h(x) = \lambda e^{\beta x} + \gamma e^{\delta x}$$

$$h'(x) = \lambda \beta e^{\beta x} + \gamma \delta e^{\delta x}$$



DI Christian Scheibböck

Next steps

- Implementation in AKIM
- Prospective studies
- Evaluating the performance of the system

DI Christian Scheibböck

Summary

- Combination of tumour markers improves accuracy of information
- Computer assisted computation of the pre-test probability
- Optimal function fitting of the survival curve

DI Christian Scheibböck