Comparison of Extrinsic and Intrinsic Dynamic Contrasts in Fast 3D Optical Mammography

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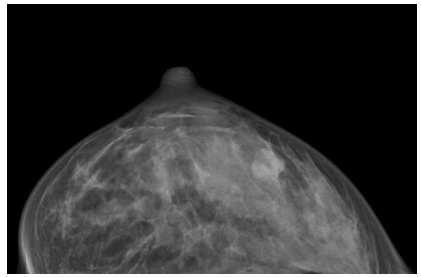
We all know this…

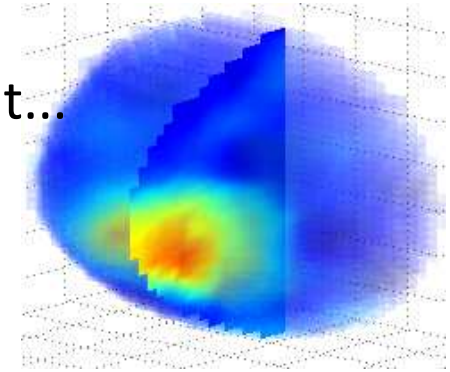
Promises of optical mammography

- Primary goal: Functional contrasts → higher sensitivity/specificity?
  → X-Ray Sens.: 75% (50%)
- Secondary goals: Safe technology, etc.



Challenges of optical mammography:

- Calibration / absolute Hb measurements are difficult
- Image reconstruction unstable
- → Technology not quite as simple/cheap as one thought...



Where are we:

- Review by Leff et al 2008:
  OM sensitivity approaching 85% in retrospective studies; large prospective database is outstanding

Our Approach: Dynamic Imaging

- **Interrogate hemodynamics:**

  Basic tissue function and physiology (neo-angiogenesis, blunted vascular response, oxygen supply/demand imbalance, extravasation, etc...)

- **Acquire time series of optical tomography images**

  (high frame rate & high dynamic range)

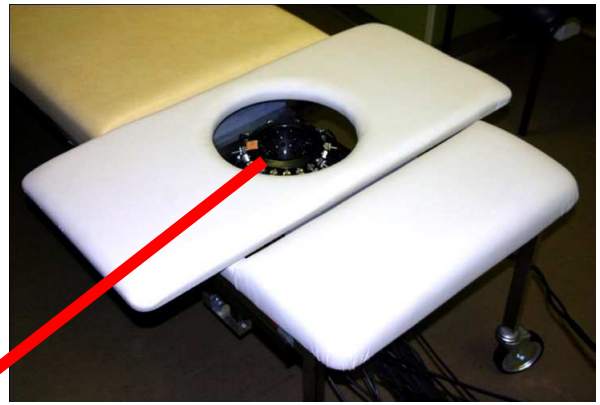
- **Stabilize the image reconstruction process:**

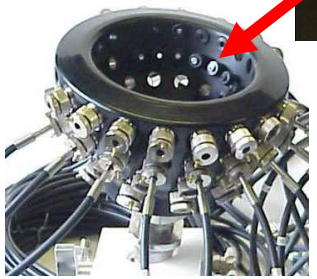
  Reconstruct relative changes, insensitive to background properties, boundary conditions

Barbour,et al, JOSA A (2001)

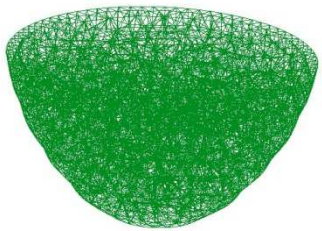
Technology

- **Scanner**:
  DYNOT 232 optical tomography system
  31 sources x 31 detectors = 931 channels
  @ 1.9 Hz





- **Reconstruction**:
  NIRx NAVI Software,
  relative absorption changes in each of
  2243 FEM nodes



C. H. Schmitz et al., *Rev. Sci. Instrum. (2002)*

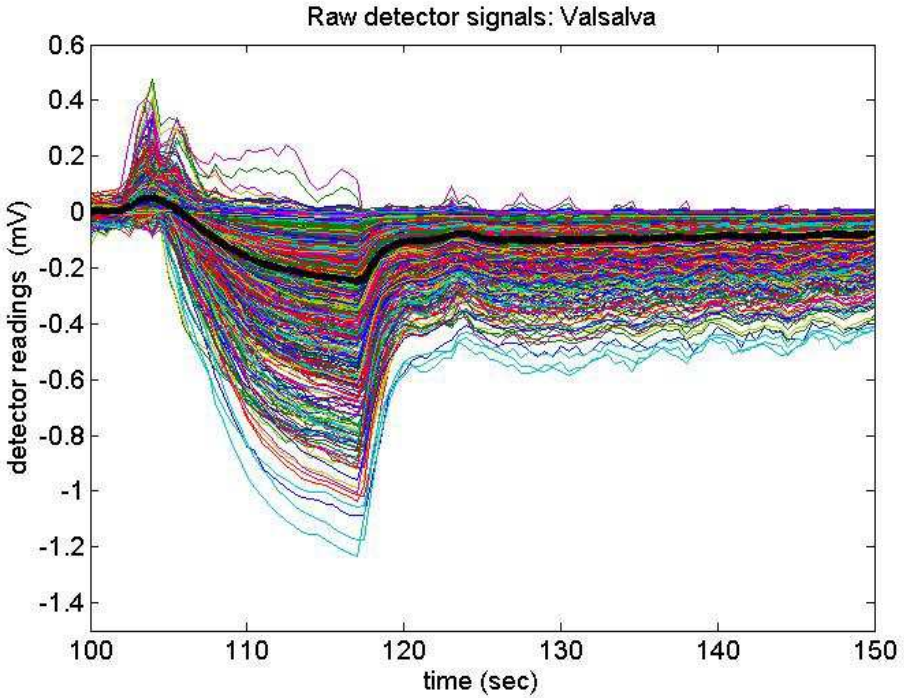
Study Design

- 30 women (mean age 53 yrs), scheduled for biopsy at Charité Radiology Clinic
- All received Gd enhanced MRI and biopsy following OM
- 19 malignant / 11 benign
- + 4 healthy controls
- **Intrinsic Contrast:**
  Valsalva Maneuver: Induce a transient increase in blood pressure
  3x Valsalva (15 sec) every 2 min.

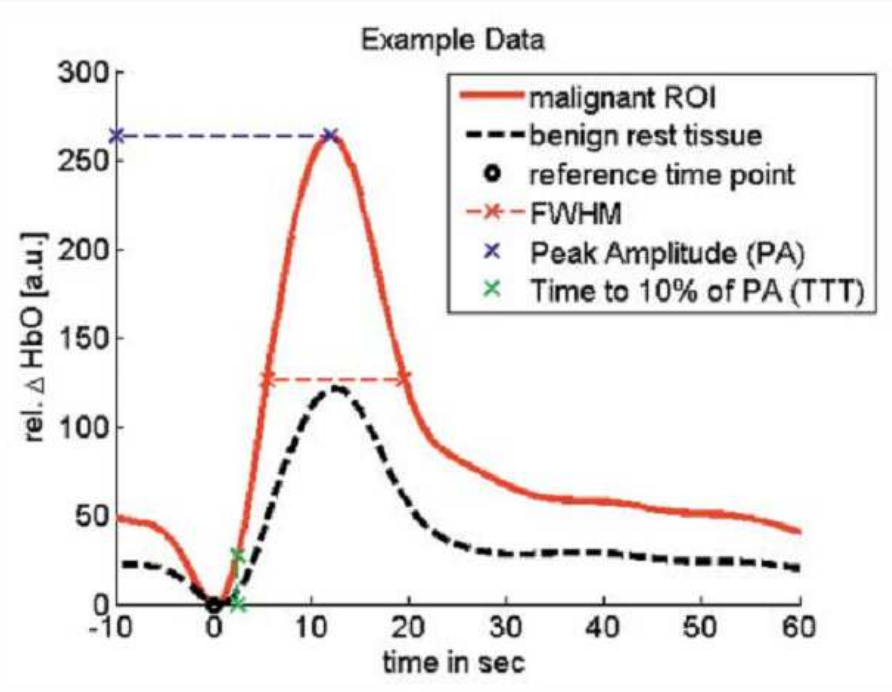
- **External Contrast Agent:** Indiocyanine Green (ICG)
  25mg ICG bolus within 5-10 sec *i.v.* (cubital vein)

Valsalva Maneuver

Raw Data



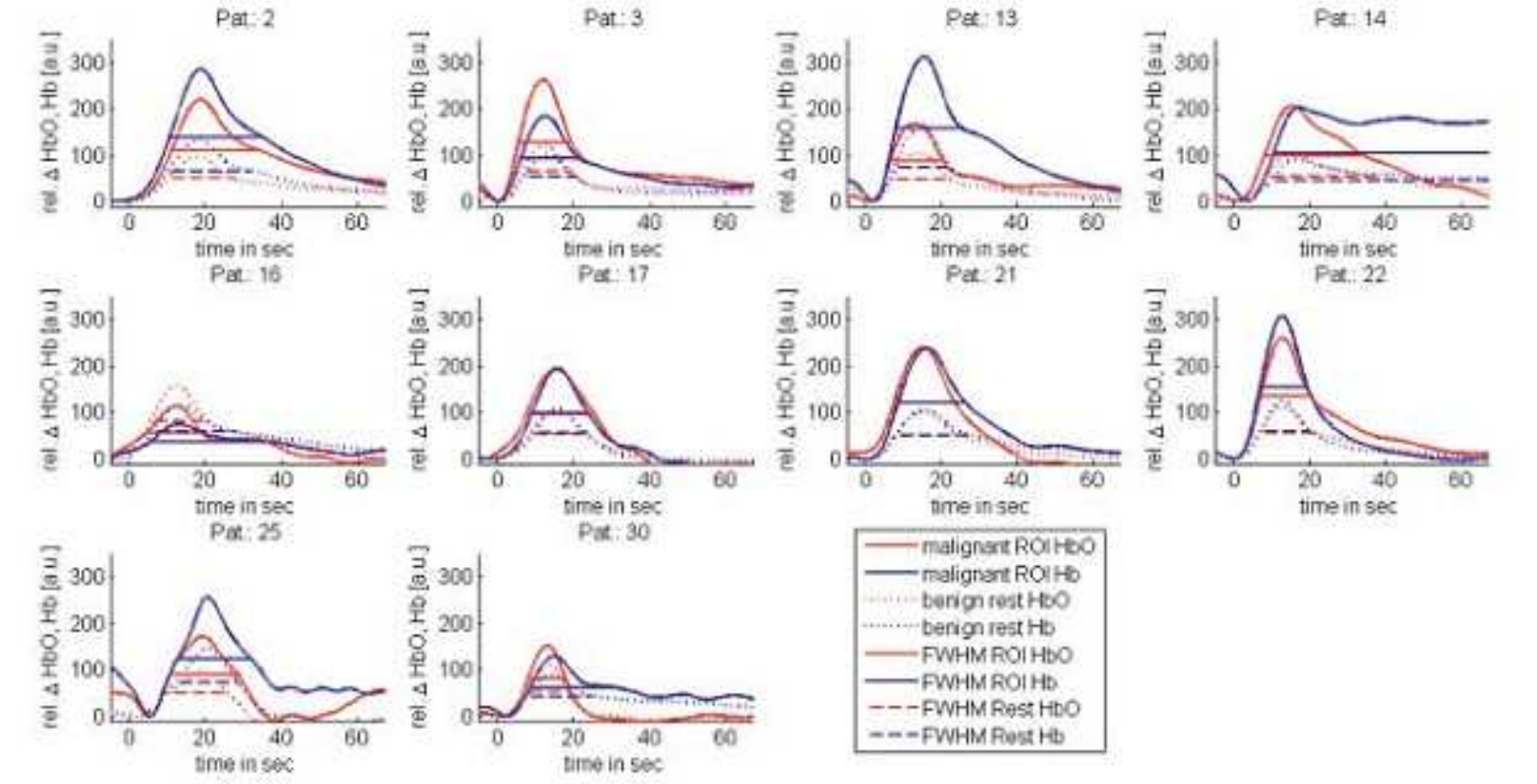
Reconstructed Data



Features examined:

- FWHM
- PA = Peak amplitude
- TTT = Time-to-Ten Percent

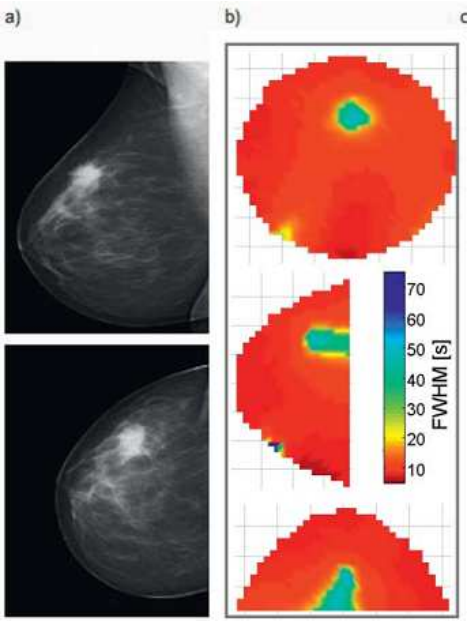
Valsalva Analysis



- Valsalva highly variable, depends strongly on individual performance
- We retained 10 malignant and 7 benign lesions for analysis
- → Reader-based evaluation of parameter maps

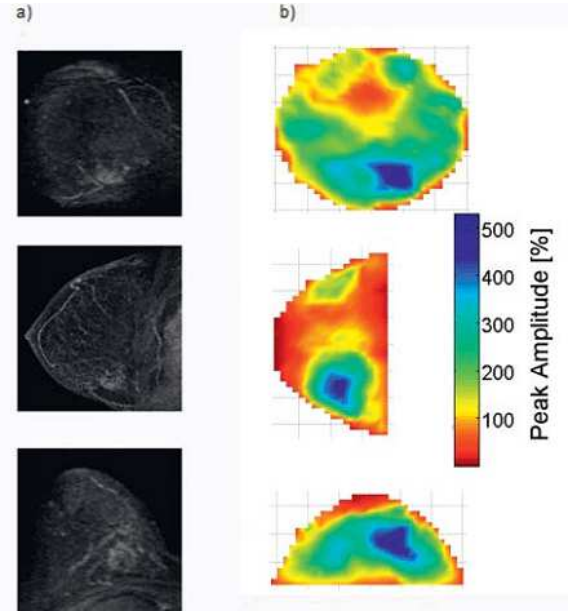
Parameter Maps

FWHM



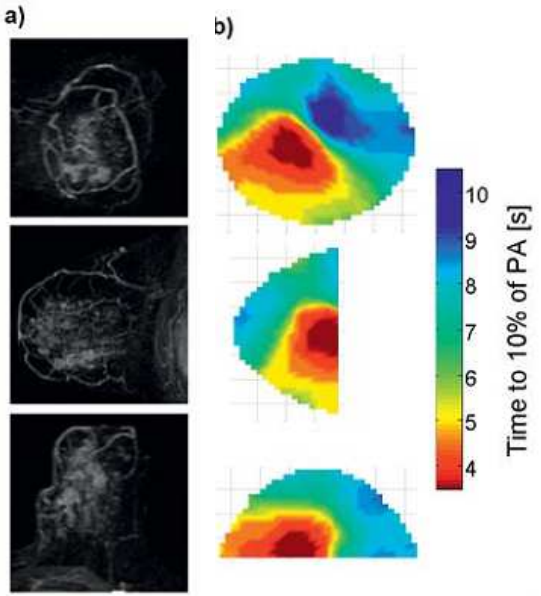
IDC, 27 mm

PA



IDC, 26 mm

TTT



DCIS, 80 mm

- Two trained readers evaluate maps (FWHM, PA, TTT, both Hb states)
- Best sensitivity ~90% (worst 50-60%)
- Findings not significant (FWHM oxy was best: p=0.057, sens 70%/spec 85%)

N. Schreiter et al. *Rofo*,184:358-366 (2012).

Evoked Responses Evaluated

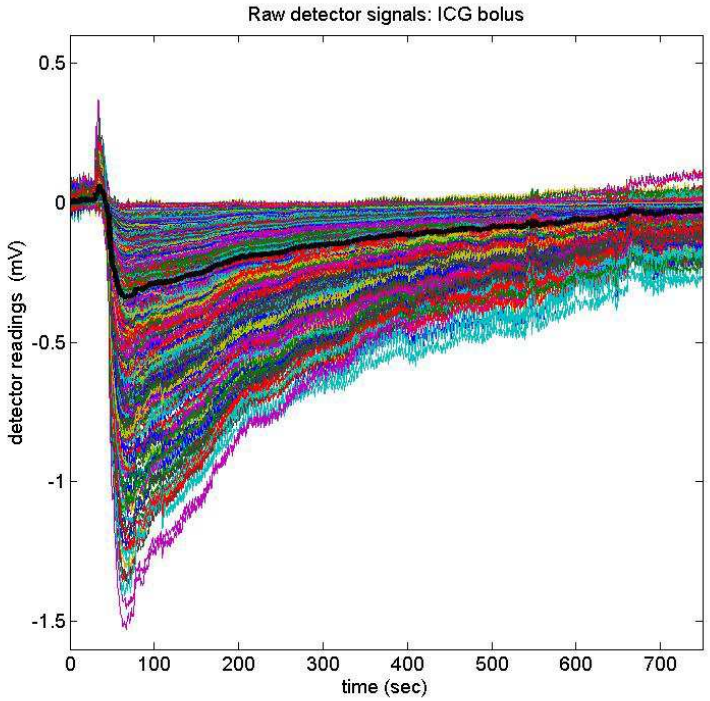
- Strong signal
- Sensitivity to pathophysiological states indicated
- Highly variable if not externally controlled

- → breathing gases (carbogen)
- → external control mechanisms
- → external modulation (pressure, ...)
- → bilateral breast imaging (self-referencing)

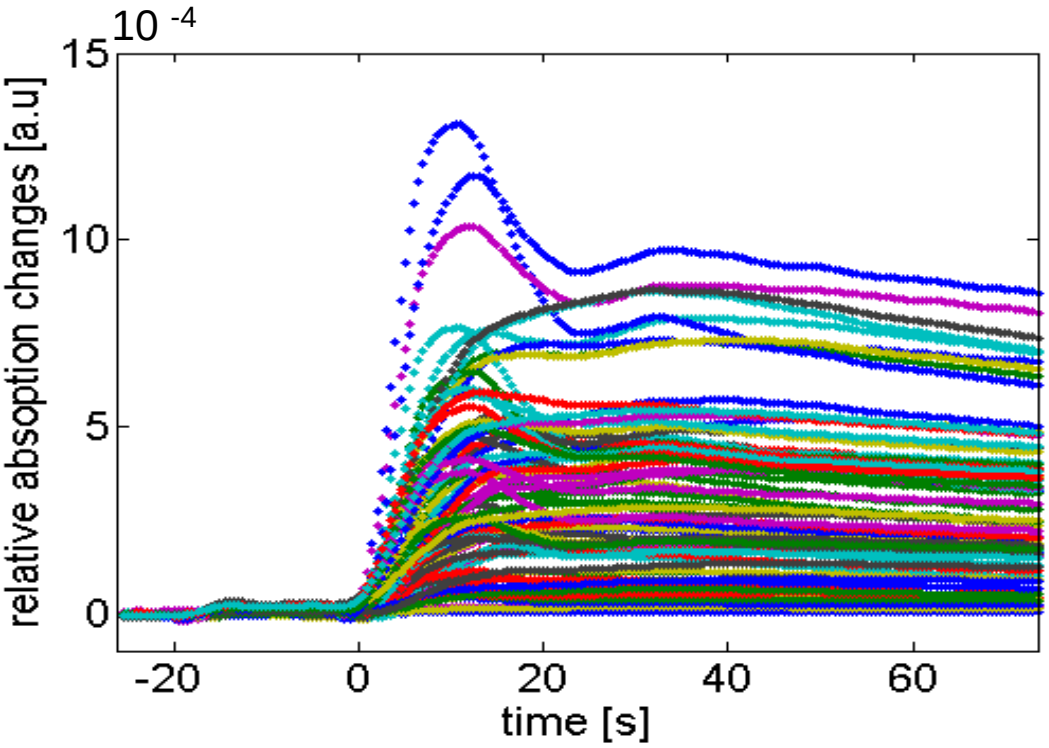
R. Al abdi et al., JOSA A (2011)

ICG Bolus Signal

Raw Data

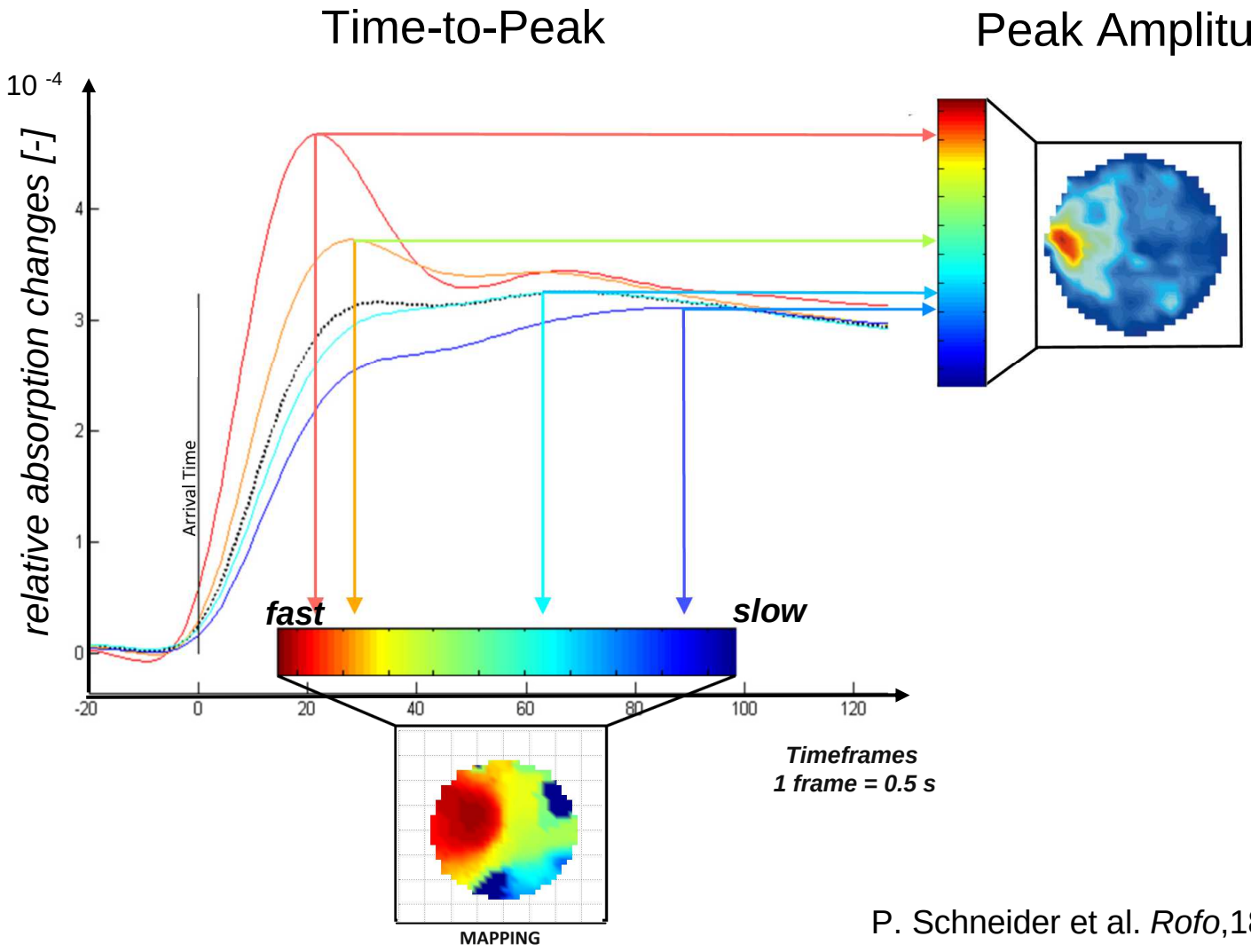


Reconstructed Data



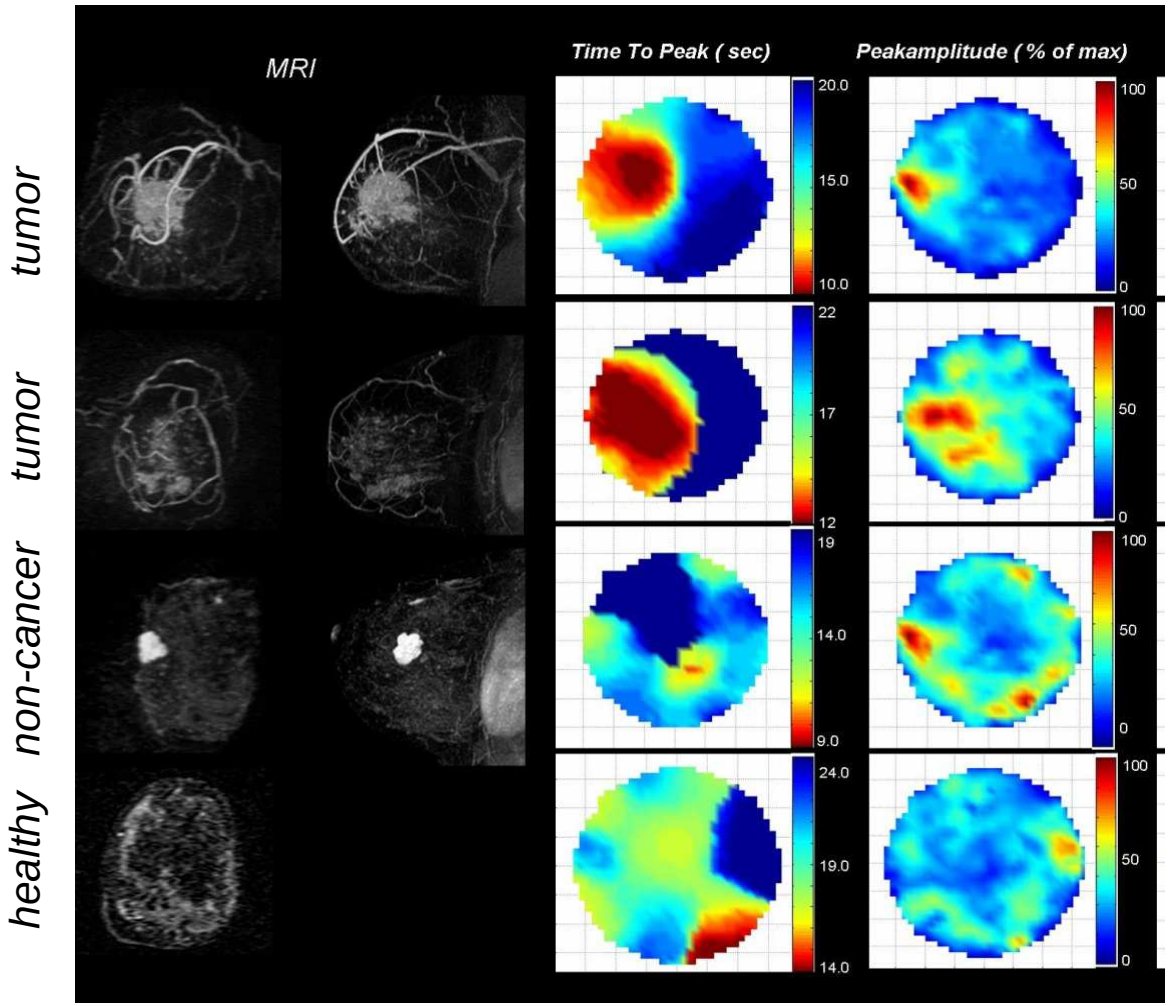
Included: 14/19 malignant, 8/11 benign

Bolus Peak Mapping



P. Schneider et al. *Rofo*,183(10):956-63 (2011)

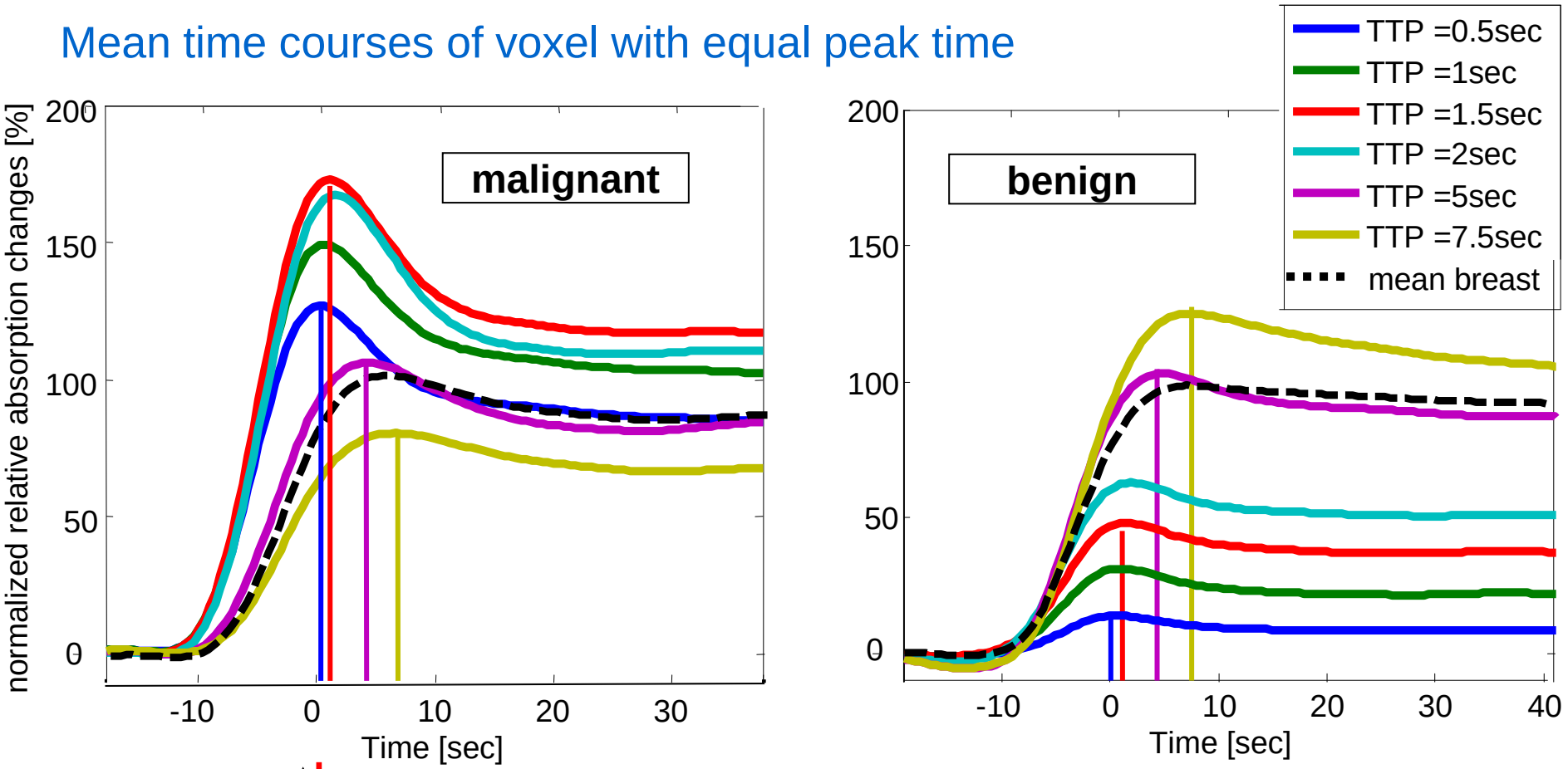
Reader- dependent visual inspection



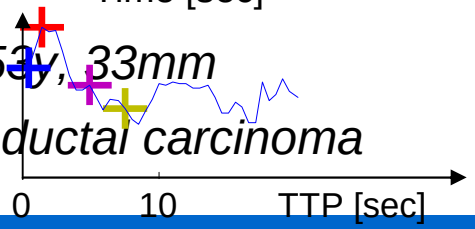
→ Reader independent tumor detection?

Peak-Time grouped Amplitude (PTA)

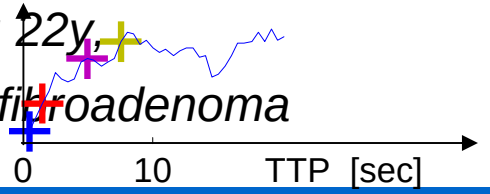
Mean time courses of voxel with equal peak time



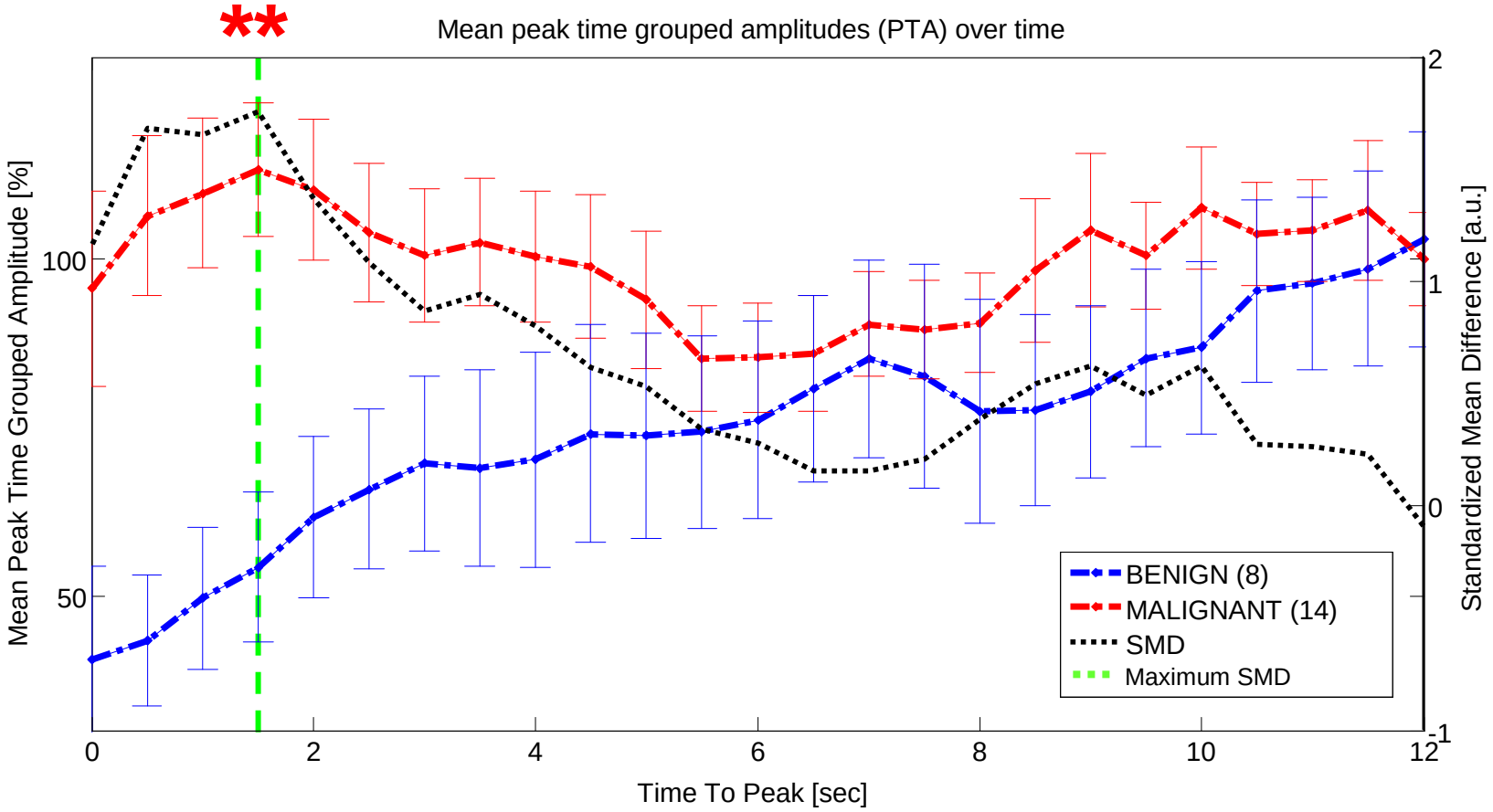
Case1: 53y, 33mm invasive ductal carcinoma



Case2: 22y, 22mm fibroadenoma

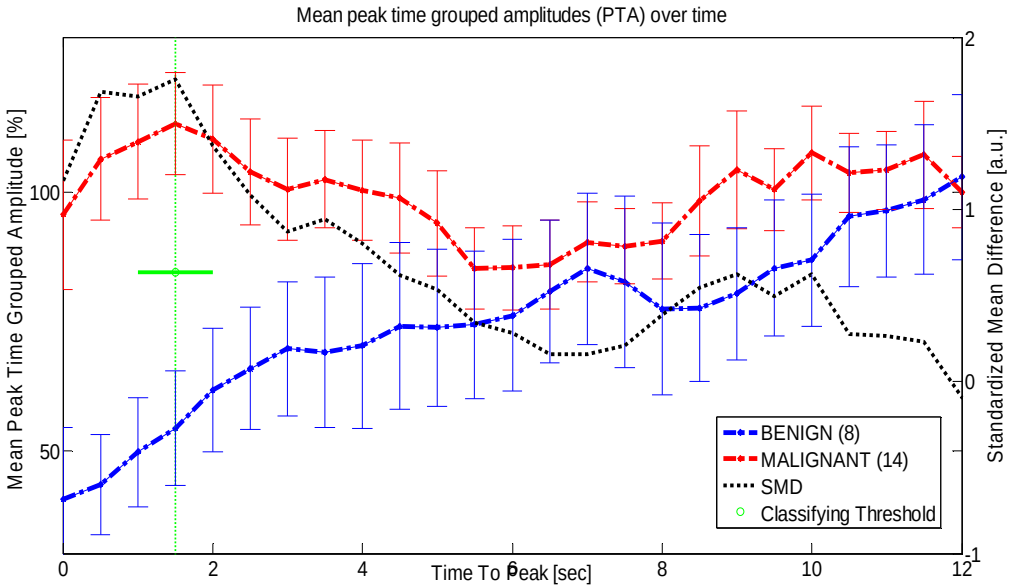


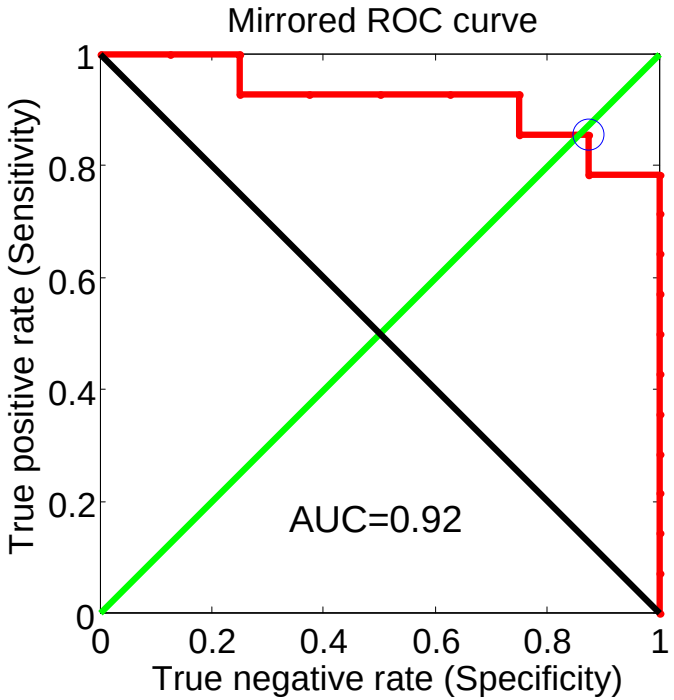
Mean PTA-curves over all patients



Significant Difference of PTA at TTP= 1.5sec between the malignant and benign lesions (Wilcoxen test, p=0.0015)

Reader independent Classification Approach





Decision Boundary for Reader Independent Classification:
PTA = 84.4% of the mean bolus signal

P. Schneider et al. *Rofo*,183(10):956-63 (2011).

Classification Rates for 22 patients

Malignant, mean lesion size (range)	Detection Rate	Benign, mean lesion size (range)	Detection Rate
Invasive ductal carcinoma , 29mm (8-51mm)	8 / 9	Fibro-cystic mastopathy, 11mm	1 / 1
Invasive lobular carcinoma, 25mm	1 / 1	Fibroadenoma, 24mm (10-51mm)	5/ 6
Invasive lobular ductal carcinoma, 17mm	0/1	Pseudoangiomatous stromalhyperplasia (PASH), (44mm)	1/ 1
Metaplastic carcinoma, 28mm (19-37mm)	2 / 2		
Ductal carcinoma in situ, 80mm	1 / 1		
Sum	**12 / 14**	**Sum**	**7/8**

Sens. = 86%

Spec. = 88%

P. Schneider et al. *Rofo*,183(10):956-63 (2011).

Conclusion

- High-frame rate DOT allows imaging fast tissue dynamics
- Intrinsic and extrinsic tumor contrasts obtainable
- Intrinsic contrast suffers from repeatability

  → requires control or reference
- Dye bolus kinetics highly replicable,

  fast uptake dynamics allow for sensitive pathological assessment

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