Titel des Beitrags:
Rapid optical imaging of human breast tumour xenografts using anti-HER2 VHHs site-directly conjugated to IRDye 800CW for image-guided surgery.

Abstract:
Molecular optical imaging using monoclonal antibodies is slow with low tumour to background ratio. We used anti-HER2 VHHs conjugated to IRDye 800CW to investigate their potential as probes for rapid optical molecular imaging of HER2-positive tumours by the determination of tumour accumulation and tumour to background levels. Three anti-HER2 VHHs (11A4, 18C3, 22G12) were selected with phage display and produced in Escherichia coli. Binding affinities of these probes to SKBR3 cells were determined before and after site-specific conjugation to IRDye 800CW. To determine the potential of VHH-IR as imaging probes, serial optical imaging studies were carried out using human SKBR3 and human MDA-MB-231 xenograft breast cancer models. Performance of the anti-HER2 VHH-IR was compared to that of trastuzumab-IR and a non-HER2-specific VHH-IR. Image-guided surgery was performed during which SKBR3 tumour was removed under the guidance of the VHH-IR signal. Site-specific conjugation of IRDye 800CW to three anti-HER2 VHHs preserved high affinity binding with the following dissociation constants (KD): 11A4 1.9 ± 0.03, 18C3 14.3 ± 1.8 and 22G12 3.2 ± 0.5 nM. Based upon different
criteria such as binding, production yield and tumour accumulation, 11A4 was selected for further studies. Comparison of 11A4-IR with trastuzumab-IR showed ~20 times faster tumour accumulation of the anti-HER2 VHH, with a much higher contrast between tumour and background tissue (11A4-IR 2.5 ± 0.3, trastuzumab-IR 1.4 ± 0.4, 4 h post-injection). 11A4-IR was demonstrated to be a useful tool in image-guided surgery. VHH-IR led to a much faster tumour accumulation with high tumour to background ratios as compared to trastuzumab-IR allowing same-day imaging for clinical investigation as well as image-guided surgery.