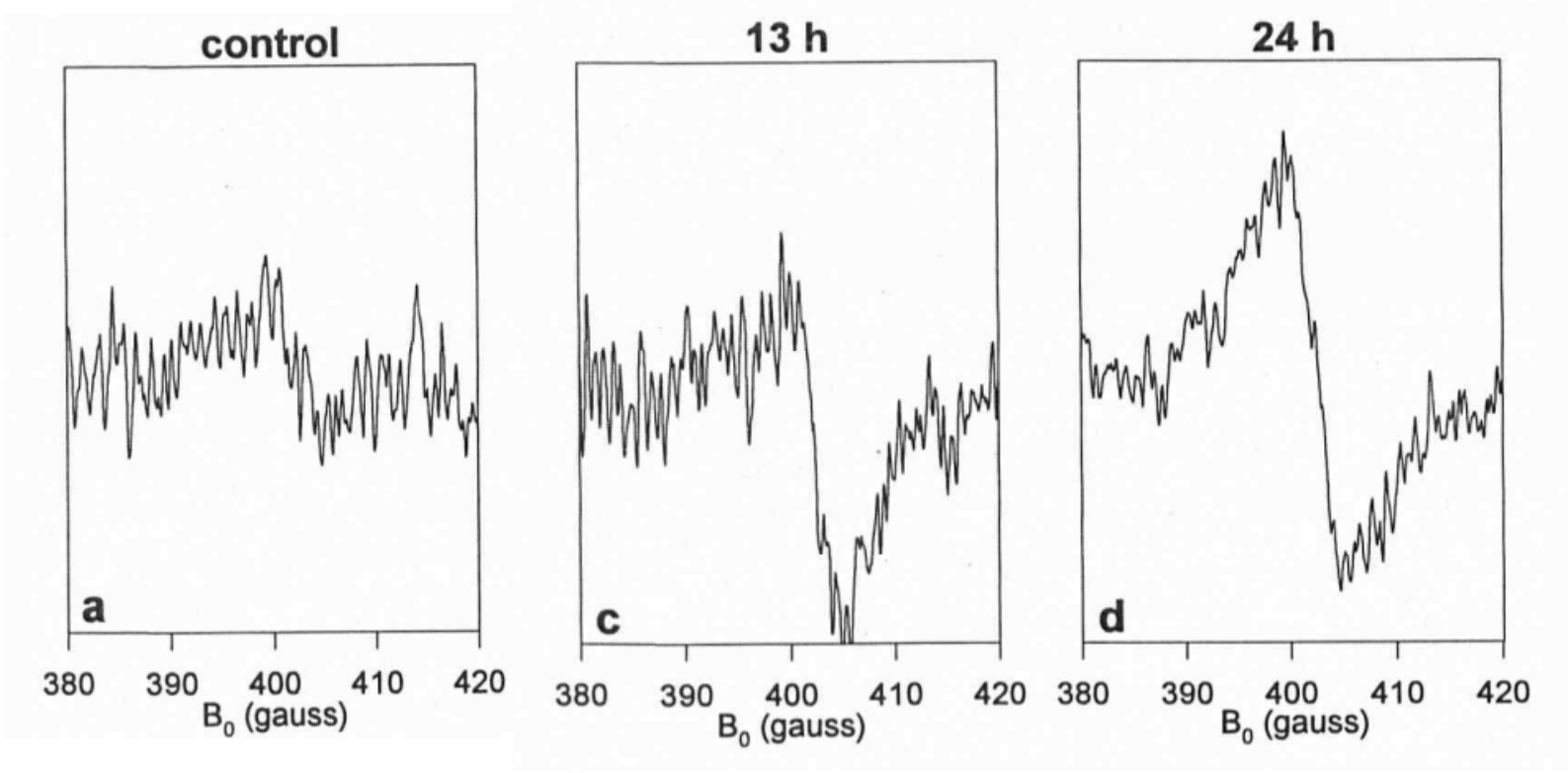
# EPR spectroscopy and imaging topical applications in vivo

**The effect of drugs**

**Purpose:** To investigate the formation of free radicals during the application of Anthralin (a drug for e.g. psoriasis).

**Results:** EPR can directly monitor drug induced radical formation under peretinent therapeutic conditions




In vivo signal from the skin of nude mice after topical applications of Anthralin.

K.Mader . G.Bačić, et al.,J.Pharmac. Sci. 86(1997)126-134.

# EPR spectroscopy and imaging  topical applications in vivo

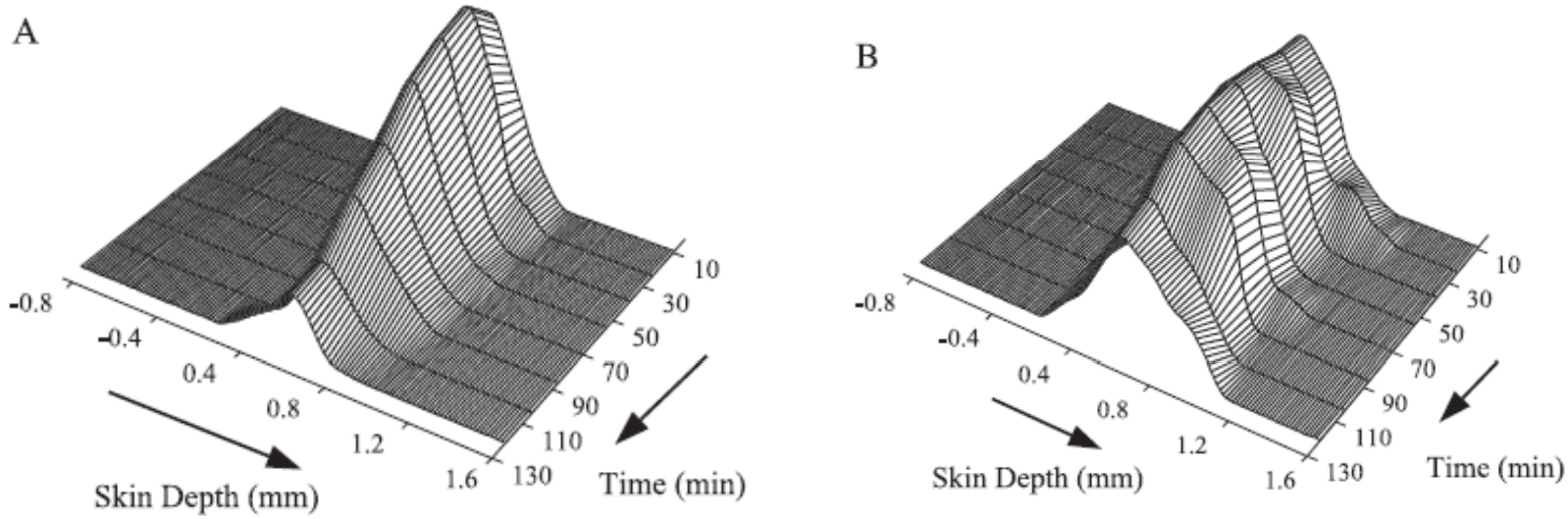
**The effect of UV light**

**Rational:** UV light presents potent oxidative stress in the skin

**Results:** UV treatment reduces the rate of reduction of nitroxide  in the skin.

control

UV-treated




1D time dependent EPR signal of nitroxide topically applied

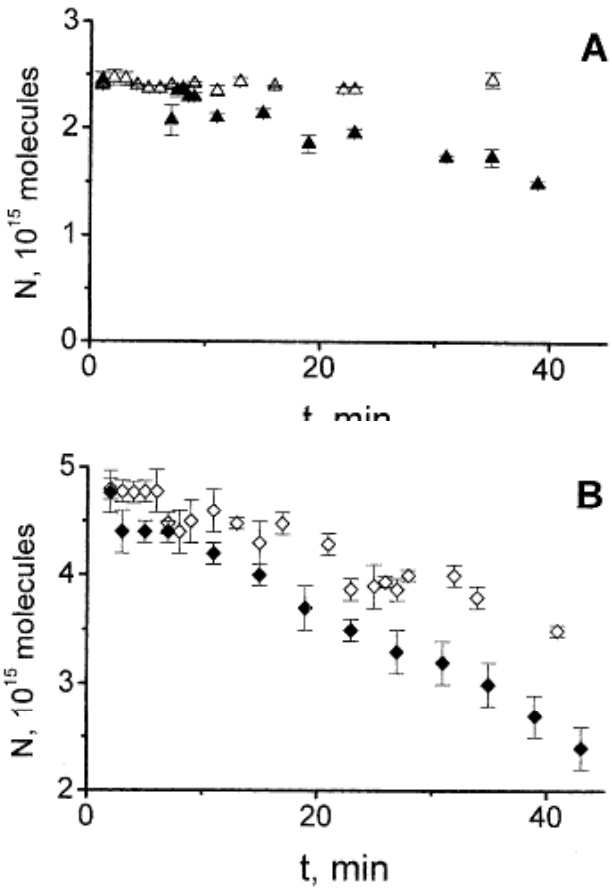
He, et al., Free Radic. Biol&Med.  36(2003)665.

# EPR spectroscopy and imaging-topical applications liposomes as delivery system

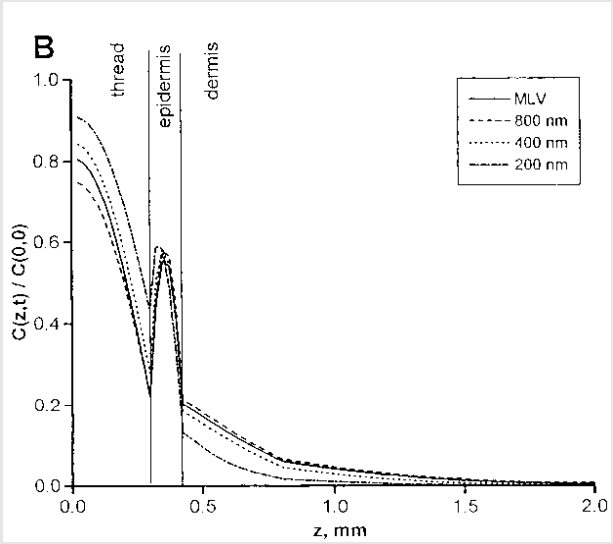
Sentjurc et al., J. Control Release 59(1999)87
Honzak et al.,J. Control Release 66(2000)221

**Aim:** Liposomes can be used to transport hydrophylic substances through the skin. Nitroxides as surogate drugs.

**Results:**
Liposomes enhance topical delivery of hydrophylic substances.The penetration depends on the composition and size of liposoms.




**Influence of vesicle size on the concentration depth distribution profile in pig ear skin.**




Niotroxide entrapped in DPPC/Cho liposomes.
X-band, 1-D gradient applied perpendicular to the skin

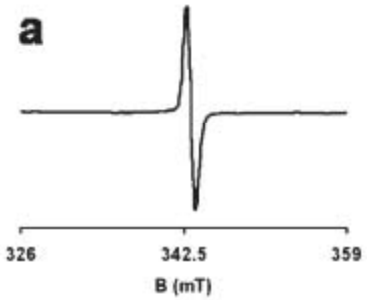
EPR spectra intensity decay of nitroxide applied as solution (A) or entraped in liposomes (B) on the skin of live nude mice (L-band).
Decay is faster with liposomes due to penetration and subsequent reduction.

# EPR spectroscopy and imaging. Topical applications - skin

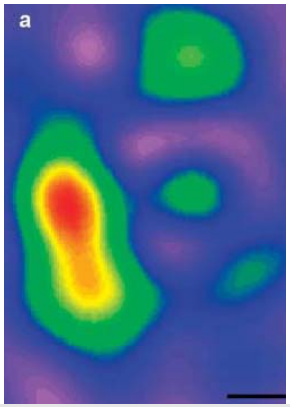
## Melanoma

**Purpose** An early detection of skin malignant melanoma at initial stage of development is critical for the outcome of the disease. Estimated 5-years survival rate is almost 100% for superficial melanoma diagnosed early but less than 10% for disseminated melanoma.

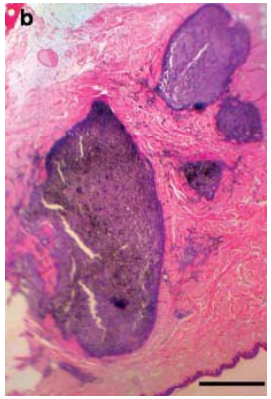
- EPR can non-invasively distinguish melanoma from mole.
- Current development of EPR spectrometers should soon bring this technology to clinics.




EPR spectra of endogenous stable free radical in melanine pigment




2D EPR L-band images of melanoma in human skin *in vitro.*



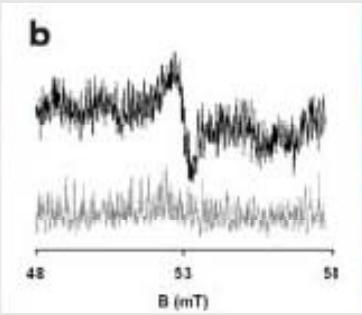

Corresponding histological section (bar = 1 mm)

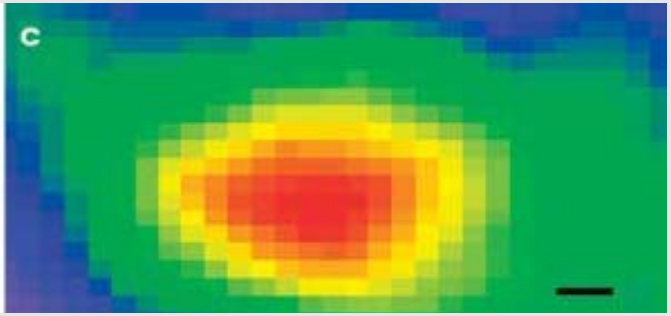
### In vivo studies of B16 melanoma in mice, L-band

Melanoma grown in subcutaneous tissue

In vivo EPR spectra with (top) and without (bottom) melanoma.

EPR image using head coil. (bar = 2 mm)

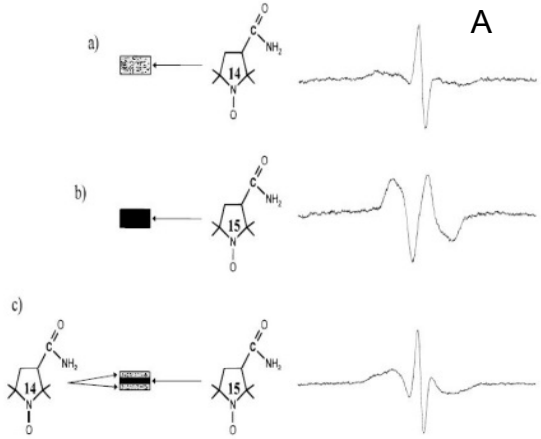




E.Vanea, et al., NMR in Biomed. 21(2008)296-300

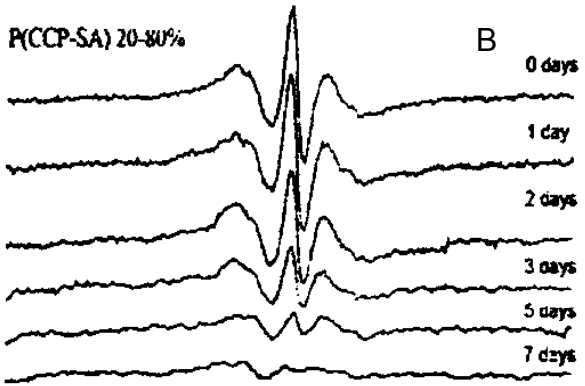
# IN VIVO SPECTROSCOPY

## Controled release from implantable devices - nitroxides as surrogate drugs - topical EPR



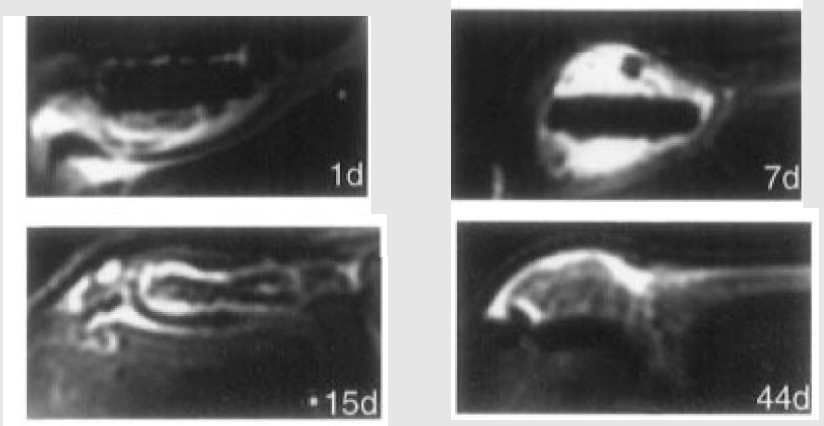

A – in vitro spectra of polimer tablets loaded with 14-N PCM (a) 15-N PCM (b) and sandwich with both.

1,2 GHz EPR surface coil over subcutaneously implanted tablet




B - In vivo elimination of nitroxides from the subcutaneously implanted tablet

### Physical destruction of the tablet as assessed by MRI




### The question

How the drug is released, i.e. whether tablets decompose by surface or bulk erosion?

### The experimental solution

Use a sandwich tablet where surface and inner part are loaded with 14- or 15-N nitroxide and follow the remaining ratio of nitroxides in the tablet.

### Conclusion

Simultaneous use of both noninvasive technologies enables detailed insight into drug release and polymer degradation

K.Mader . G.Bačić, et al., J. Pharmac. Sci. 86(1997)126134.