Novel treatments in nanomedicine: Developments and challenges

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Cyclops Grand Challenge Workshop

What's wrong with nanomedicines?

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Development of nanomedicines is a key component of next generation therapeutics, but scientists still don't fully understand how key parameters drive efficacy

Material	Delivery efficiency [%ID]	No. Data Sets
Inorganic	0.8	86
Organic	0.6	137
Inorganic material		
Gold	1.0	45
Iron oxide	0.6	8
Other	0.9	23
Targeting strategy		
Passive	0.6	175
Active	0.9	57

1. Median 0.7% Injected dose reached tumour

2. This number has not changed in 10 years!

The problem: There is no internal measure of predicting efficacy for individual patients; all patients get a nominal dose and treatment regime

Chan et al. 2016, Nature Reviews "Analysis of Nanoparticle delivery to tumours"

Beyond targeting, addressing efficacy

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Challenges in Nanomedicine translation – towards closed loop therapeutics and personalisation of medicine

Theranostics

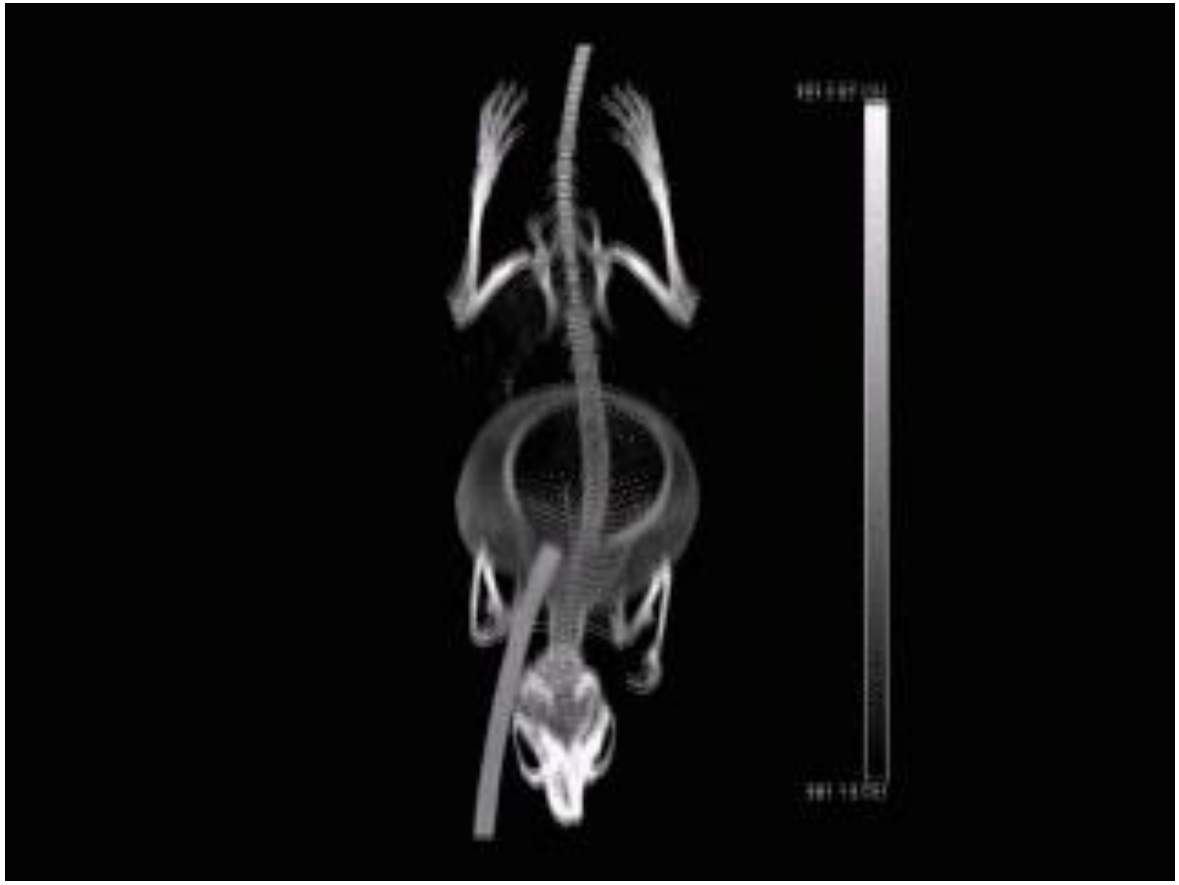
Wirelessly relay information back to clinician in real-time, allowing analysis and comparison with big datasets and drive therapeutic decisions

Dynamic PET

Liver

Heart

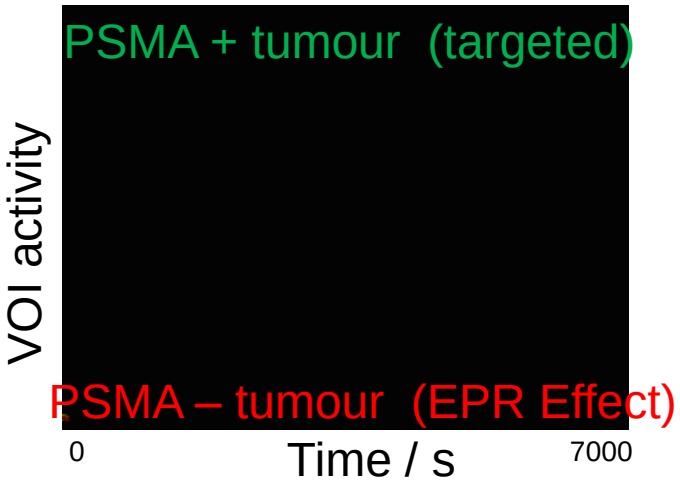
Kidney



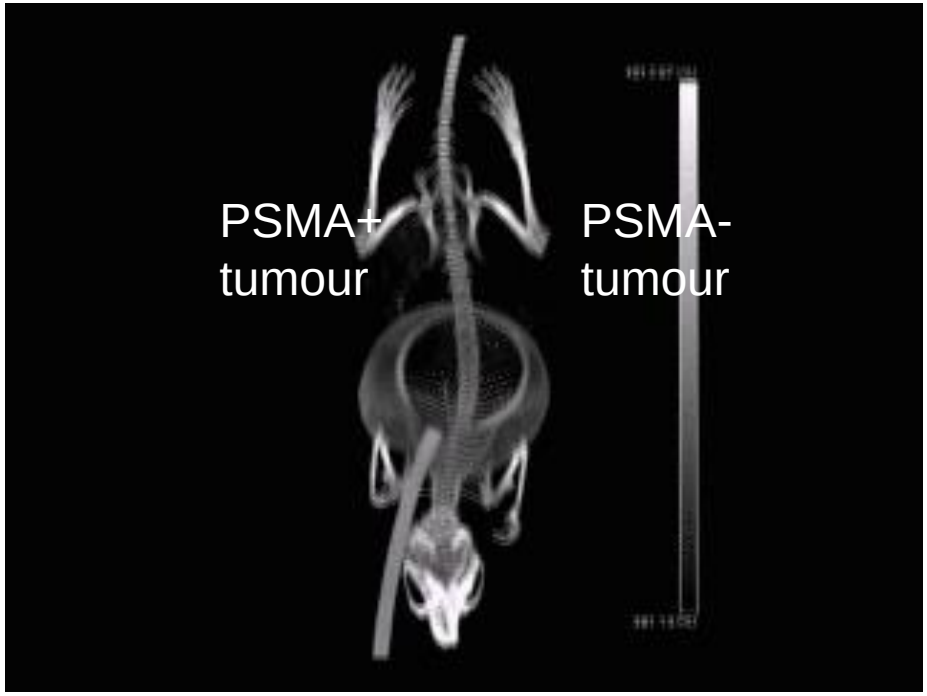
First 2 hours following injection of nanomedicine

2 hrs

Imaging nanomedicine aggregation in tumour



Time-activity curves for tumours



Dynamic PET with CT

Our Approach for optimising treatment: Two compartment model for tumour aggregation of nanomedicines.

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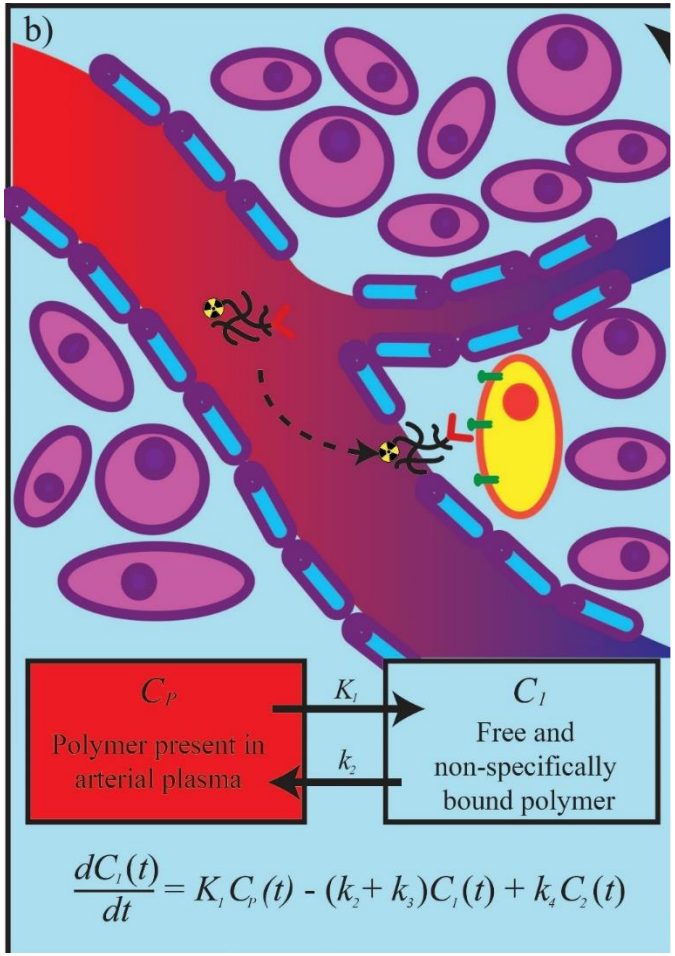
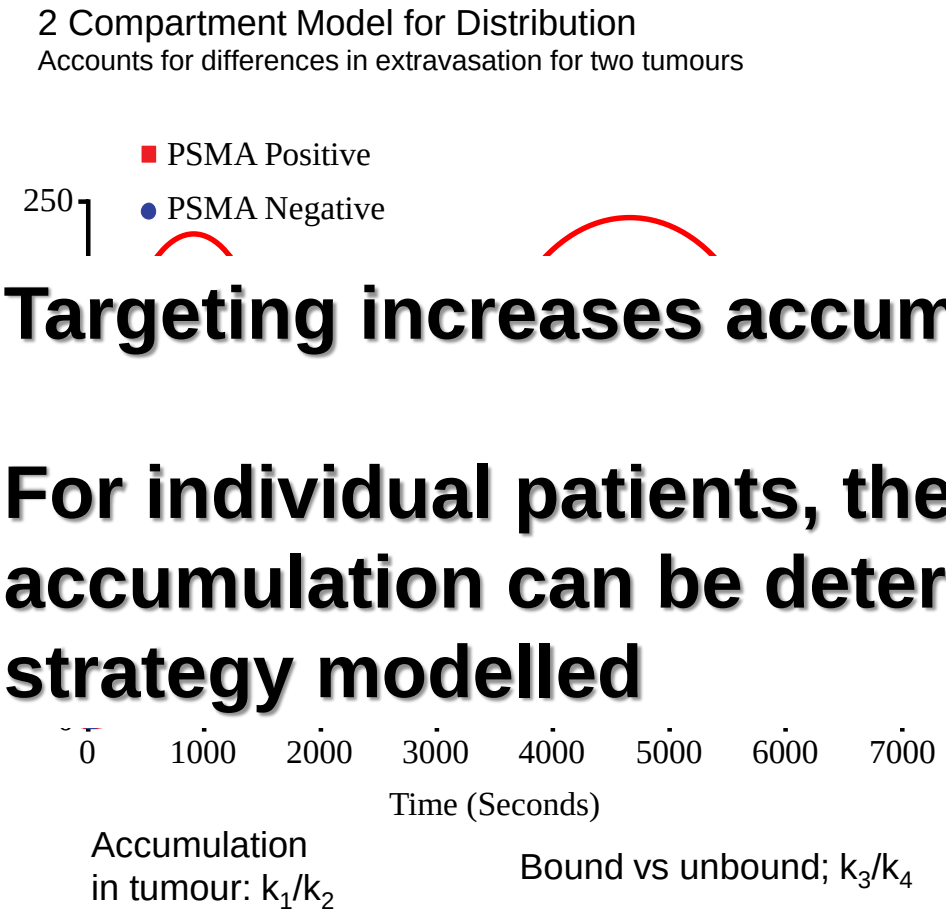


Nanomedicine distribution in tumour – targeted vs EPR effect



Targeting increases accumulation by ~ 2-fold

For individual patients, the degree of accumulation can be determined and therapeutic strategy modelled

Accumulation in tumour: k_1/k_2

Bound vs unbound; k_3/k_4

Strategy 2: Feedback loop on therapeutic response, rather than delivery

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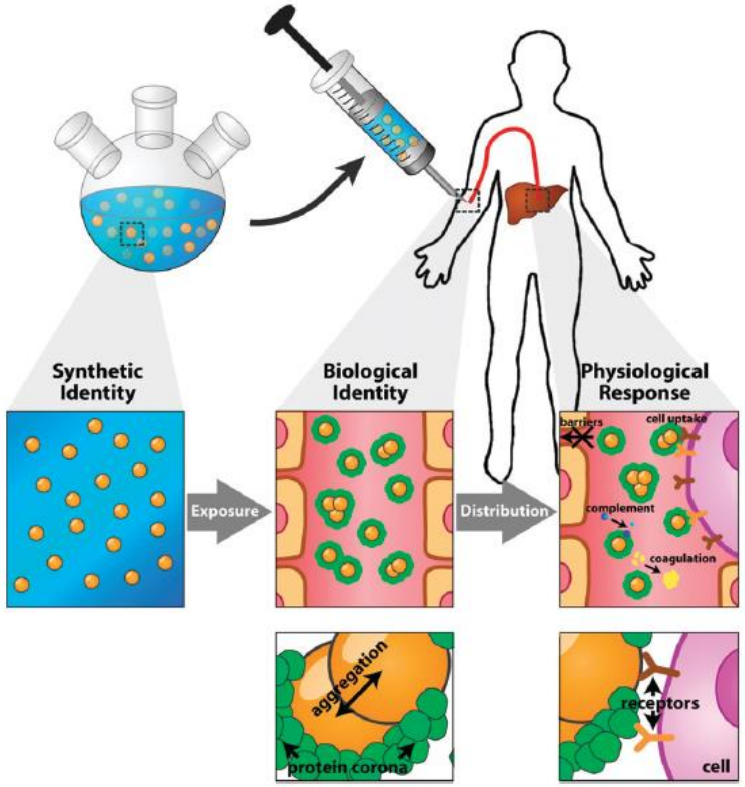
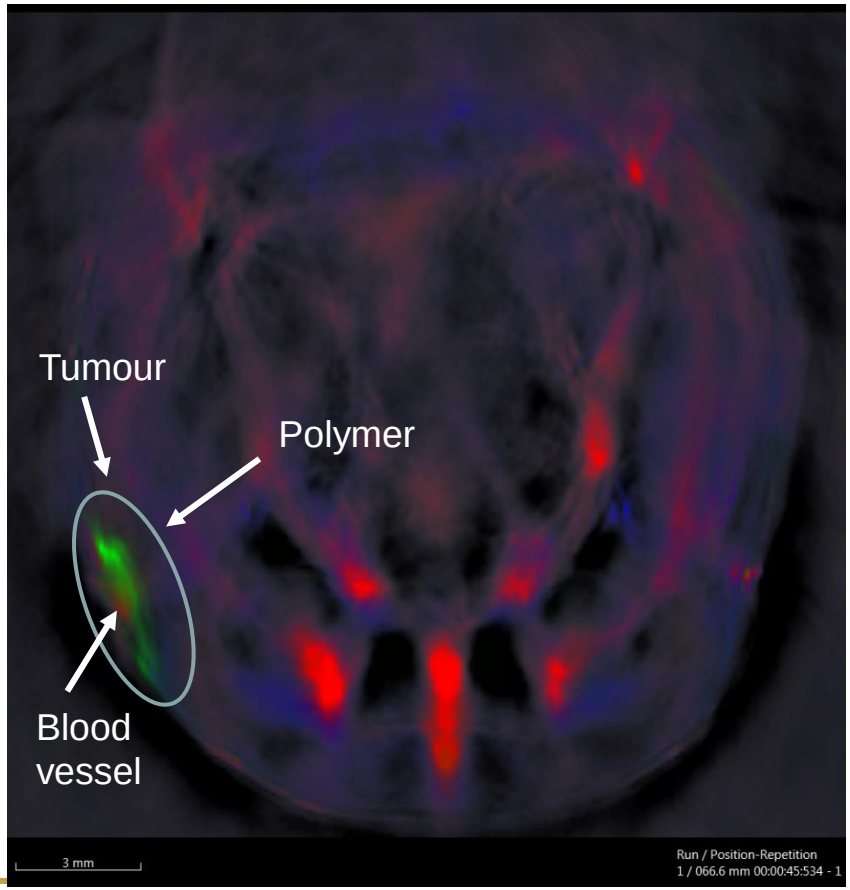
Variable patient response to treatment and dose



Theranostic materials that are activated by response (apoptosis)



Strategy 2: Feedback loop on therapeutic response, rather than delivery

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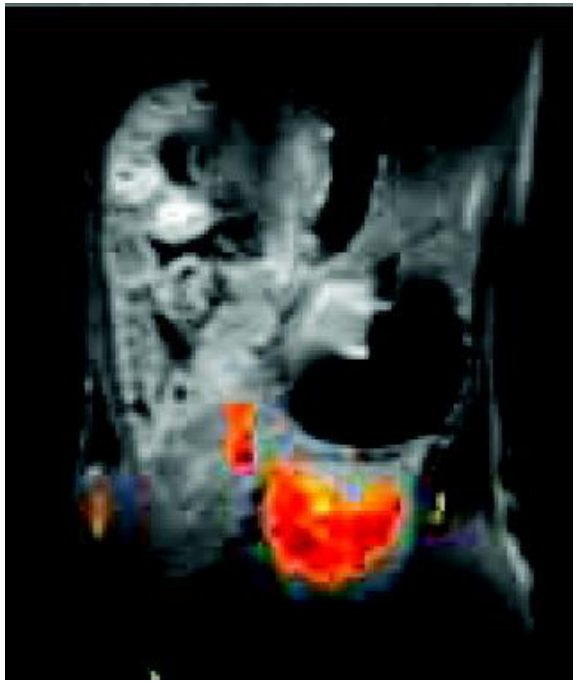
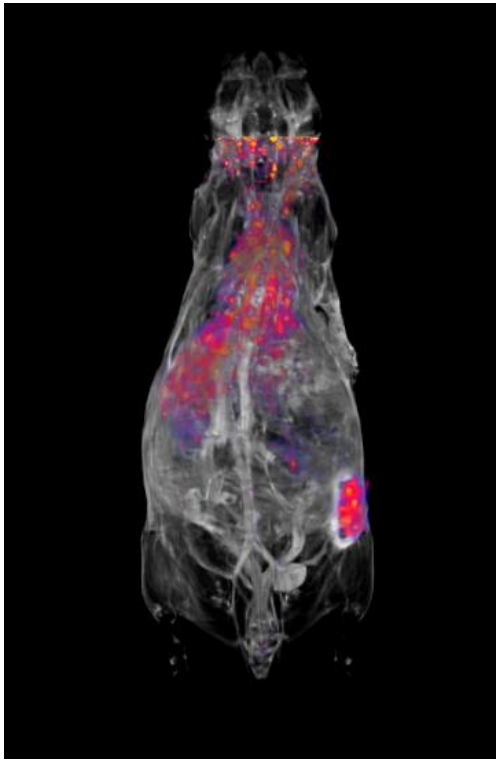
Switchable theranostics – Combined ^{19}F MRI/^{1}H MRI



Multimodal Imaging – looking at multiple responses simultaneously



Summary

New approaches to nanomedicines offers a route for developing internal feedback mechanism for therapeutic efficacy; theranostics

Challenges lie in detection, and choosing suitable response probes; subsequent decision making can be guided by feedback loop to established data sets.

With suitable modelling, these systems offer a realtime validation of individualised treatments.