Nanoscale Imaging Probes for Personalized Medicine

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Nanotechnology for Solid Tumors

Many nanotherapeutics are currently under clinical evaluation or in clinical use (clinicaltrials.gov)...

The promise...

- Multi-functionality
  - Targeting
  - Non-invasive tracking
  - Diagnostic and therapeutic capabilities
- Promise of personalized nanotherapy
FACT: Nanocarriers need to get to the tumors to do their ‘magic’...!!

Long Blood Residence Time

Repeating passage through tumor’s microvascular bed

Enhanced accumulation in "leaky" vasculature

Enhanced Permeation & Retention phenomenon

Each tumor is different

Some tumors are not “leaky”

No prior knowledge of tumor’s status to optimize therapy protocol; type of systemic chemotherapy, dosimetry and dose frequency

Currently... One dose fits all
Multifunctional agent for patient-specific therapy: A nanoscale probe and a drug-carrier

In each specific patient, is their tumor susceptible to nano-therapy?

Our approach: Develop a nano-construct capable of:
1. non-invasive interrogation of tumor status using CT or MRI and
2. delivery of chemotherapeutics to tumor

Pre-treatment
CT/MR scan
- Nanoscale probe
- CT or MR scan
- Nanocarrier tumor distribution

CRITERION
Good candidate for Nano-therapy

Treatment
-Nanocarrier with contrast agent & drug
-Monitor treatment

Consider alternative treatments

YES

NO

Adjust dosage/frequency for optimal result
PERSONALIZED BREAST CANCER DIAGNOSIS AND THERAPY USING THE NCTX IMAGING NANOPROBE

Contrast Agent and/or Drug

50-100nm

t_{1/2} \sim 55\text{hrs}
100\text{nm} \text{ diameters}
150 \text{ mg/mL} \text{ of Iodine}
Breast cancer statistics...
most common cancer in women
- Every 3 min. a woman is diagnosed with breast cancer
- Breast cancer incidence: from 1 in 20 (in 1960) to 1 in 8 (today)
- NCI estimates for 2007: 178,000 new cases / 41,000 deaths

Mammography: most common screening tool
- Mammography is a low cost x-ray
- Annual mammogram >40 yrs
- Mammograms have caused a dramatic reduction of mortality
‘Nano-probing’ using mammography

Cell line: 13762 MAT B III rat mammary adenocarcinoma
Fisher F344 rat

Breast tumor
‘Nano-probing’ using mammography

Dose: 800 mg Liposomal Iodine / Kg body weight
‘Nano-probing’ using mammography

Dose: 200 mg Liposomal Iodine / Kg body weight

Liposomes
in tumor

Liposomes
in spleen

No vasculature
enhancement

Different
animal
Time course monitoring
Prediction of chemotherapeutic efficacy using the NCTX
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**Prediction of chemotherapeutic efficacy using the NCTX**

\[ y = -0.576x + 0.174 \]

\[ R^2 = 0.838 \]
Prediction of chemotherapeutic efficacy using the NCTX

![Graph showing prediction of chemotherapeutic efficacy](image)

- Good prognosis
- Bad prognosis

Grey level variation vs. Days after tumor inoculation

- p<0.0001
- p=0.0009
Prediction of chemotherapeutic efficacy using the NCTX

![Graph showing tumor volume over time with different treatments and prognoses.](attachment:graph.png)
Conclusions

- Nanotherapy can enable personalized tumor therapy by facilitating real-time imaging of pharmacokinetics and tumor probing in patients.

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