



Bio-applications of nanodiamonds



Jean-Charles ARNAULT
Research Director



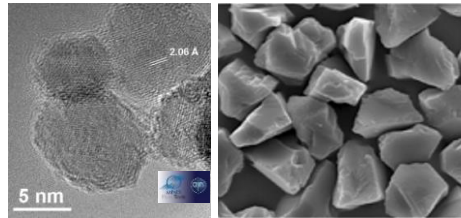
CEA LIST, Diamond Sensors Laboratory, F-91191 Gif-sur-Yvette, France

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June 12, 2019

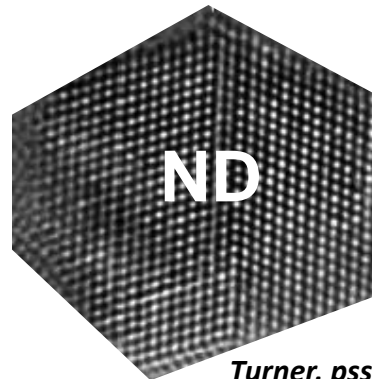
NANODIAMONDS FOR BIO-APPLICATIONS

Size (5-100 nm)



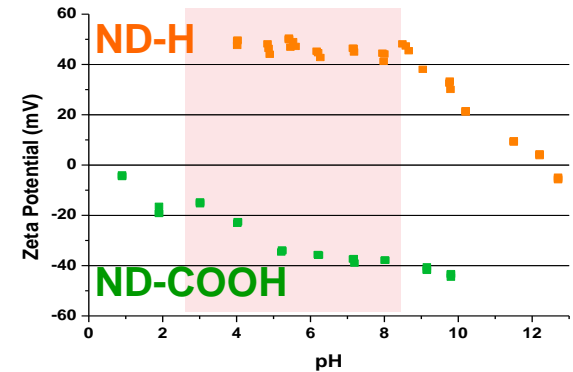
detonation

HPHT



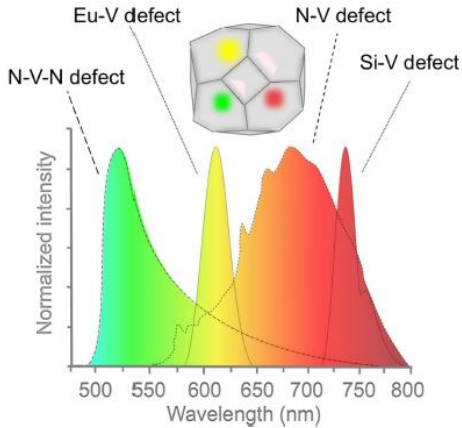
Turner, pssa (2013)

Tunable surface charge



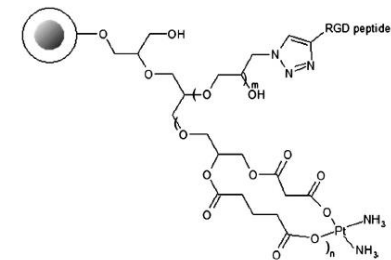
Petit et al. Nanoscale (2013)

Color centers



Turcheniuk & Mochalin Nanotechnology (2017)

Functionalization



Krüger in Nanodiamonds Elsevier (2017)

Negative ref for toxicity

Research article

Journal of Applied Toxicology

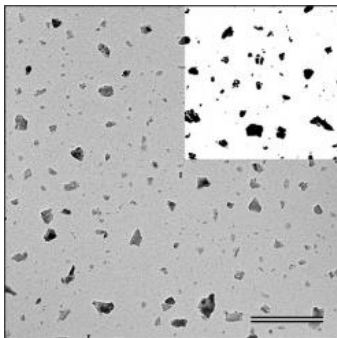
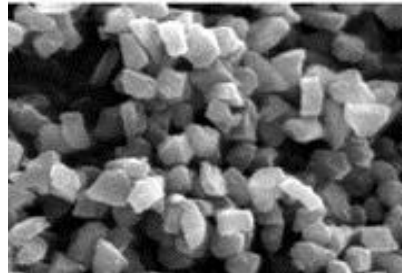
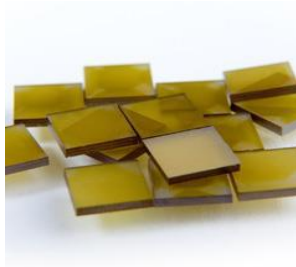
Received: 17 October 2016 | Revised: 19 December 2016 | Accepted: 26 December 2016 | Published online in Wiley Online Library: 6 February 2017
(wileyonlinelibrary.com) DOI: 10.1002/jat.3443

Carboxylated nanodiamonds can be used as negative reference in *in vitro* nanogenotoxicity studies

H. Moche^{a,b,c,t}, V. Paget^{d,t}, D. Chevalier^c, E. Lorge^b, N. Claude^b, H. A. Girard^b, J. C. Arnault^e, S. Chevillard^{d,†} and F. Nesslany^{a,c,†}

NANODIAMOND MATERIALS

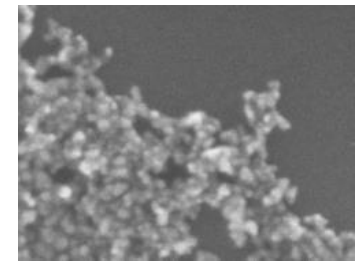
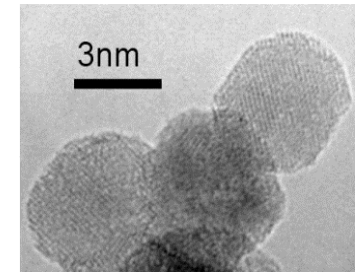
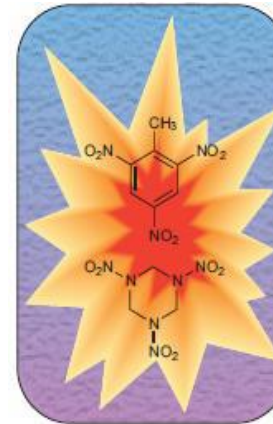
Milling of diamond



*Rehor et al.
Diam Relat Mater 2014*

- High crystalline quality
- Faceted
- Tunable diameter (10 nm → 5 μm)
- Polydispersity

Detonation synthesis



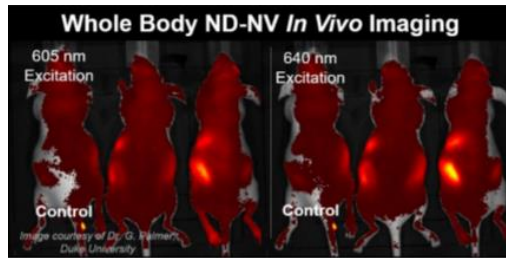
Mochalin et al. Nat Nanotech 2011

- Monodispersed
- Quasi - spherical
- Diameter (2-8 nm)
- Aggregation

Available, 1\$ per gram

Imaging

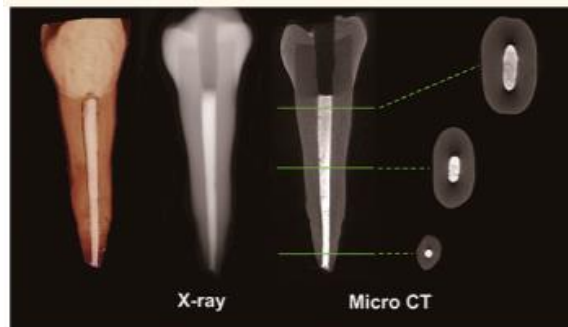
Cell tracking
MRI contrast agent



Biocompatibility
Surface chemistry
Size
Color centers

Implants

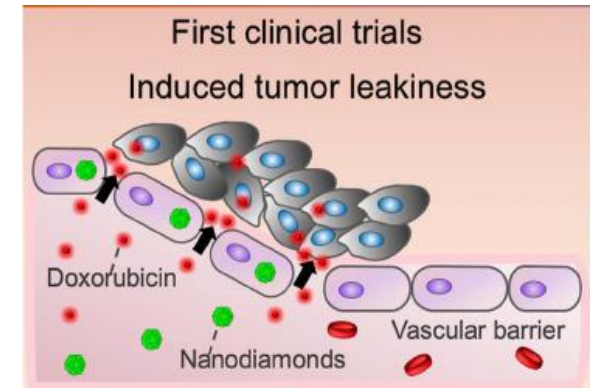
Canal therapy
Bone engineering



Biocompatibility
Surface chemistry
Mechanical properties

Drug delivery

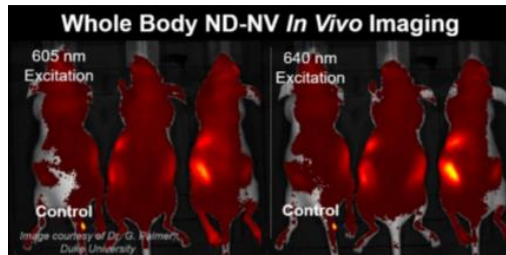
Cocktail of drugs



Biocompatibility
Surface chemistry
Size

Imaging

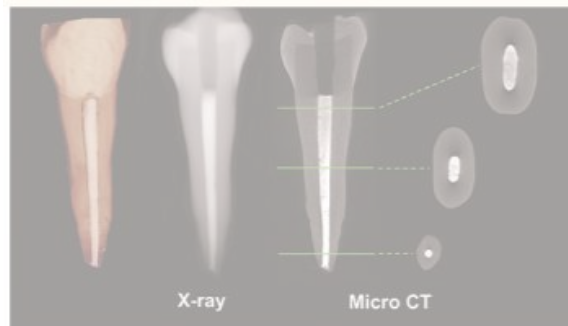
Cell tracking
MRI contrast agent



Biocompatibility
Surface chemistry
Size
Color centers

Implants

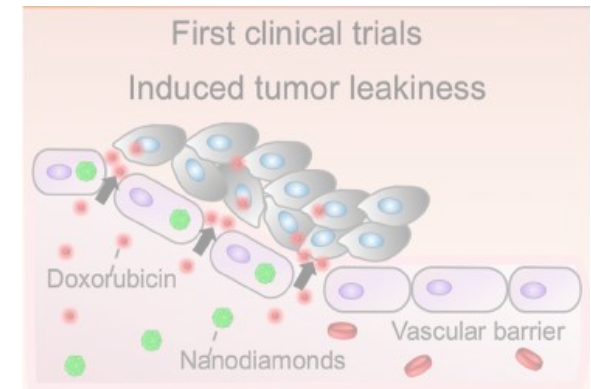
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Bone engineering



Biocompatibility
Surface chemistry
Mechanical properties

Drug delivery

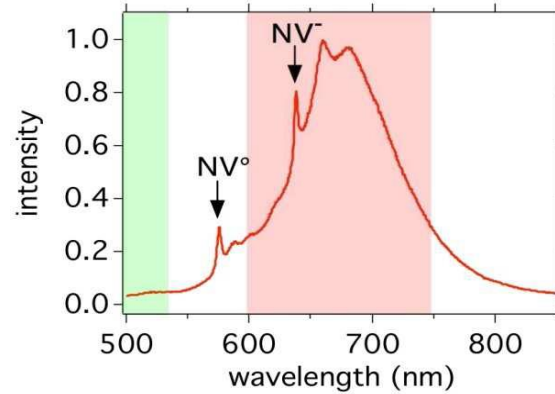
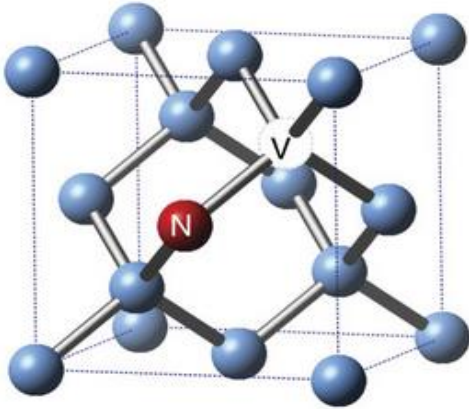
Cocktail of drugs



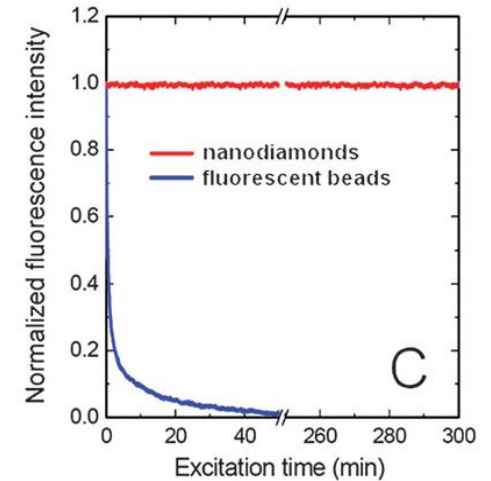
Biocompatibility
Surface chemistry
Size

SINGLE PARTICLE TRACKING

Biocompatibility
Surface chemistry
Size
Color centers

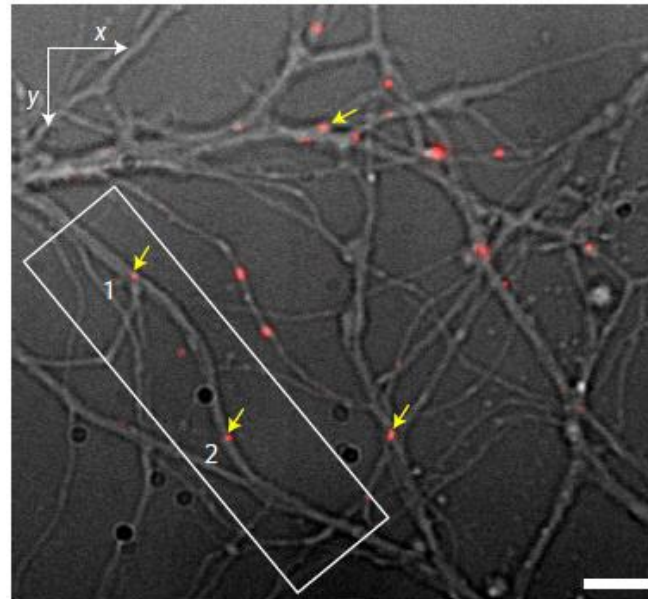


Bar-Gill et al, Nat. Comm. 3 (2012)



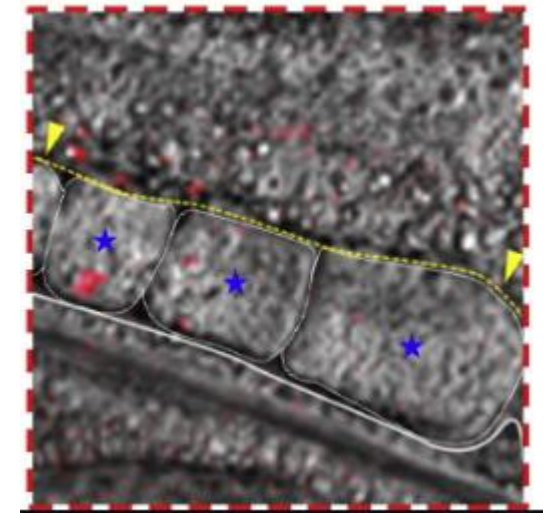
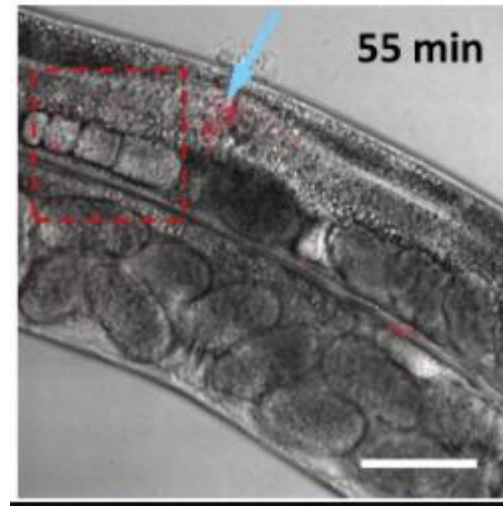
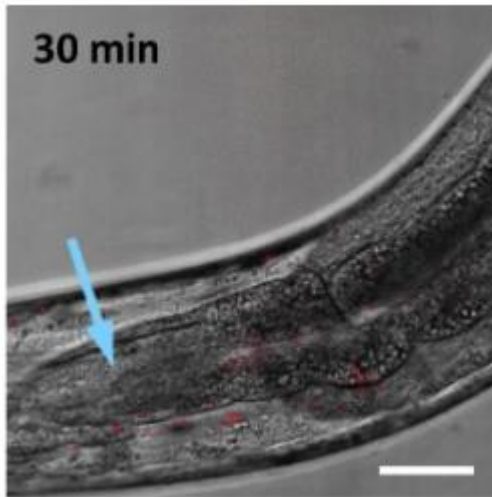
Wee et al, DRM 18 (2009)

Intraneuronal transport (*in vitro*)



spatial resolution 12 nm
temporal resolution 50 ms

Haziza et al.,
Nature Nanotechnology (2016)

Inter-cellular transport of single yolk-protein-conjugated FND in *C. elegans*.

Kuo et al, Biomaterials 2013

Long term in vivo imaging

FND-containing oocytes could be fertilized and developed into embryos

MRI CONTRAST AGENT

Biocompatibility
Surface chemistry
Size
Color centers

(a) **T1 contrast** Spin-lattice



Paramagnetic defects

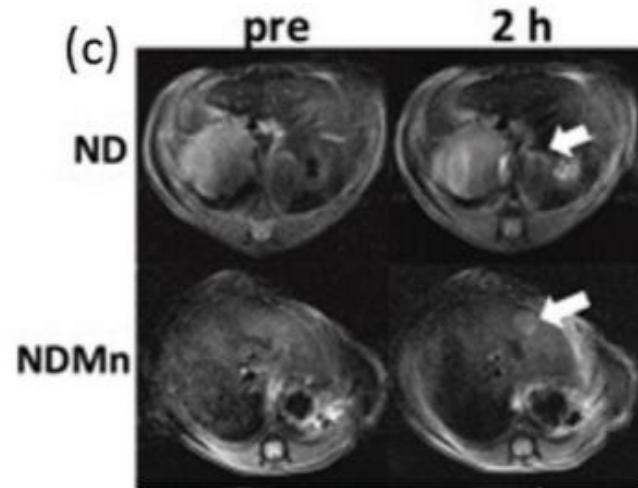
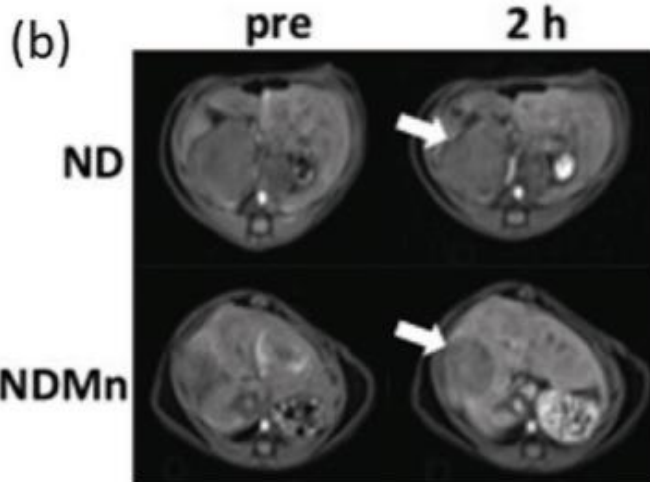


Coating with conventional Contrast agent

T2 contrast Spin-spin



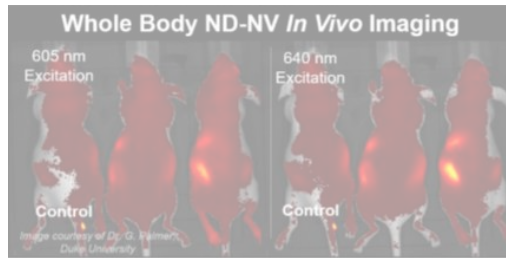
Ferromagnetic metal impurities



Tumor in mice liver

Imaging

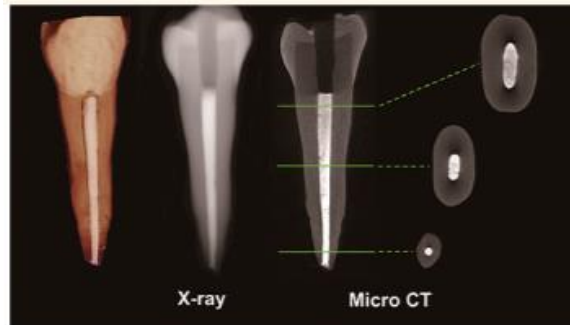
Cell tracking
MRI contrast agent



Biocompatibility
Surface chemistry
Size
Color centers

Implants

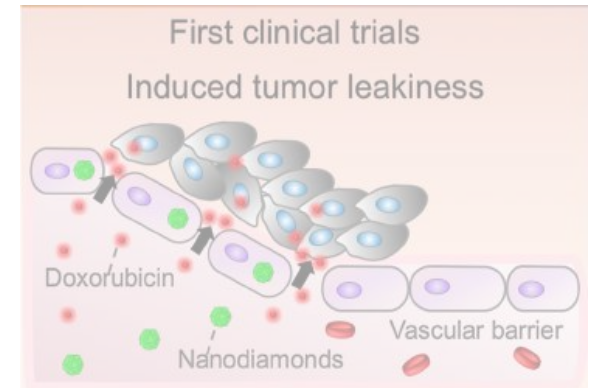
Canal therapy
Bone engineering



Biocompatibility
Surface chemistry
Mechanical properties

Drug delivery

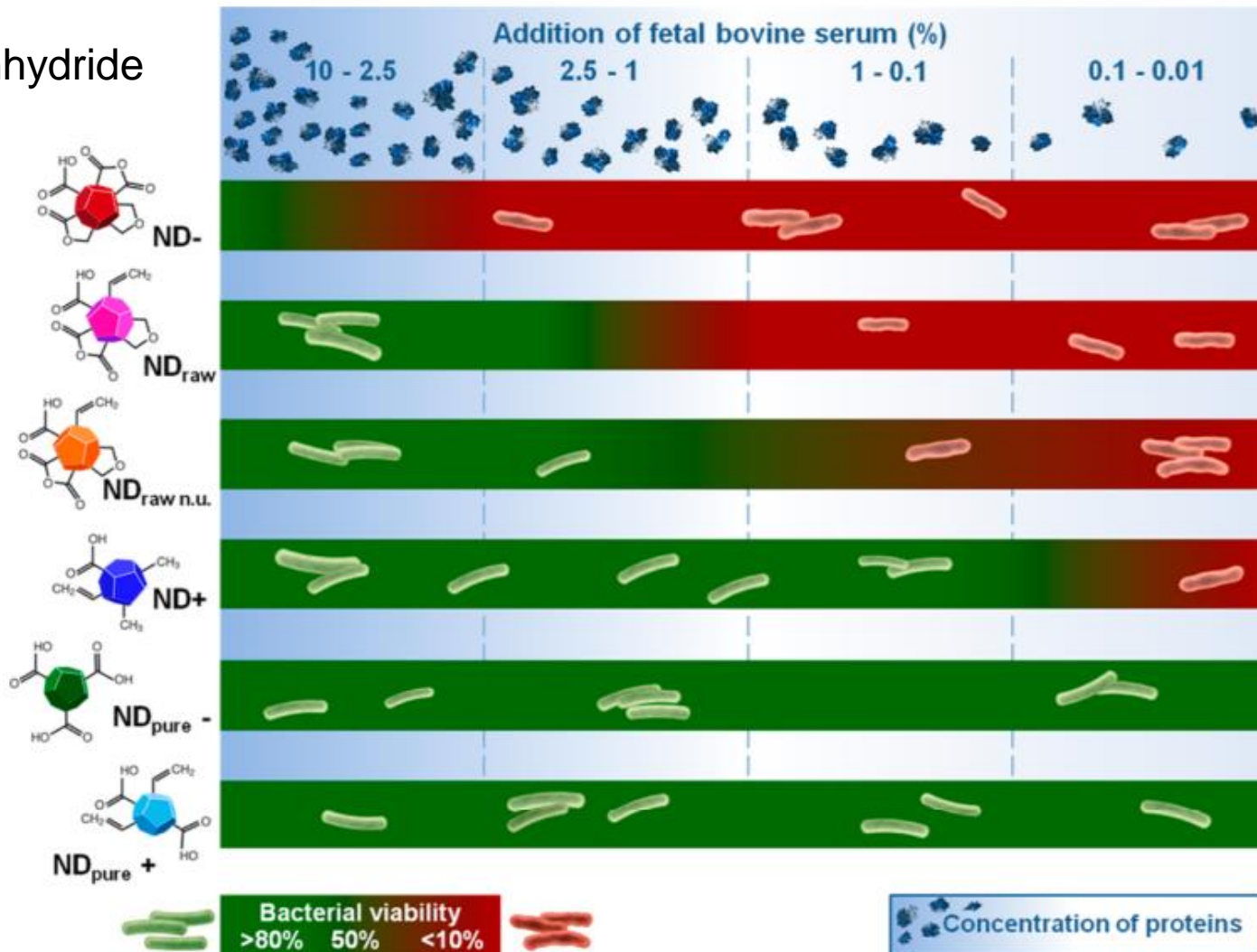
Cocktail of drugs



Biocompatibility
Surface chemistry
Size

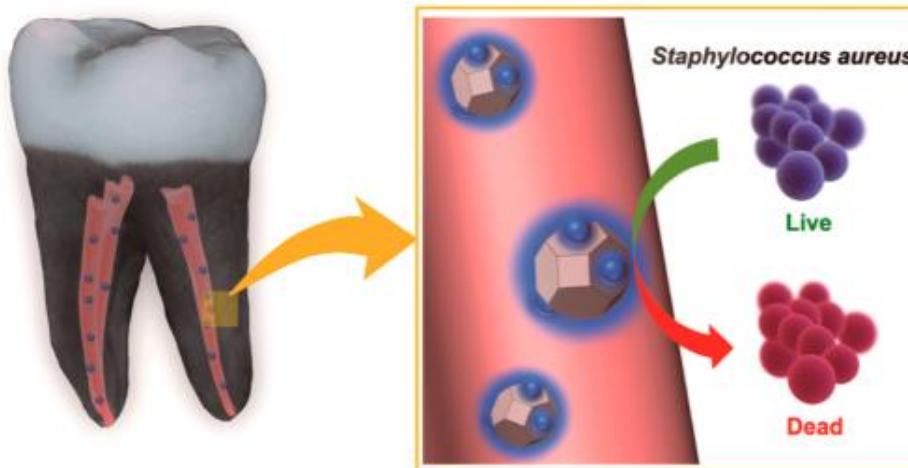
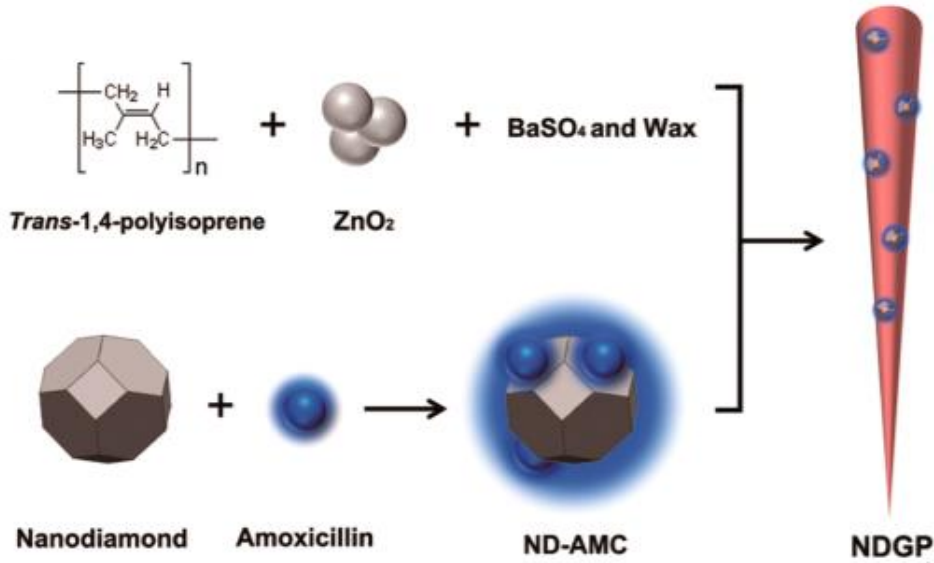
ANTIBACTERIAL PROPERTIES

acid anhydride groups

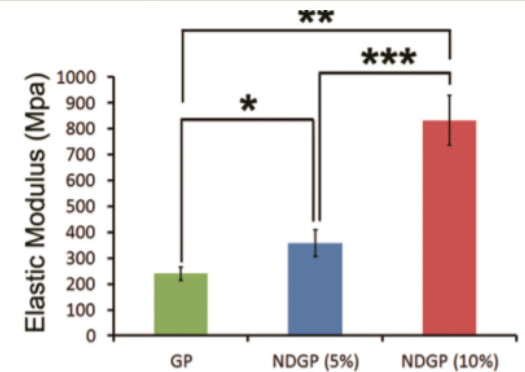
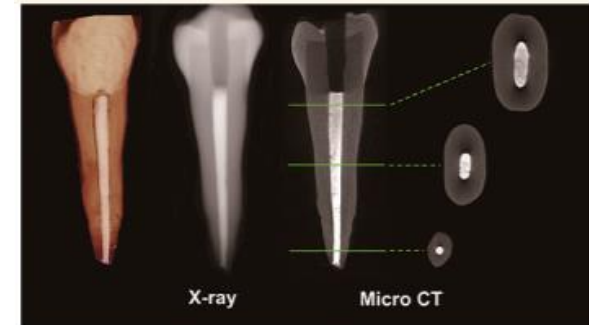


ROOT CANAL THERAPY

Biocompatibility
Surface chemistry
Mechanical prop.



gutta percha with nanodiamonds



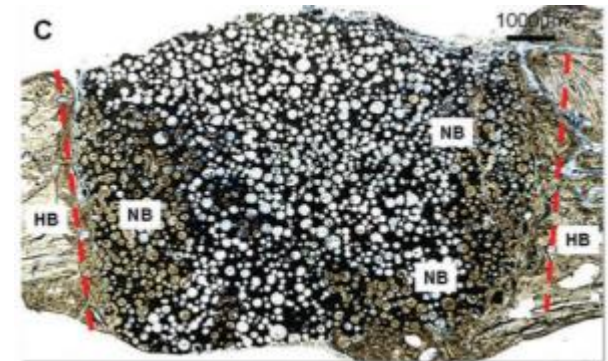
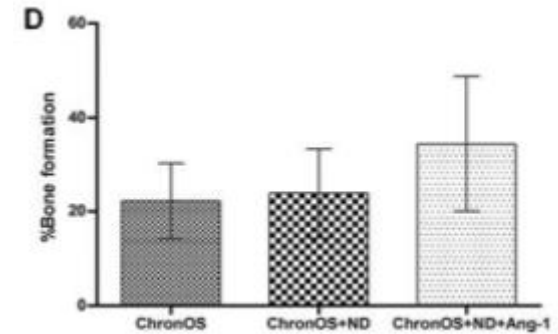
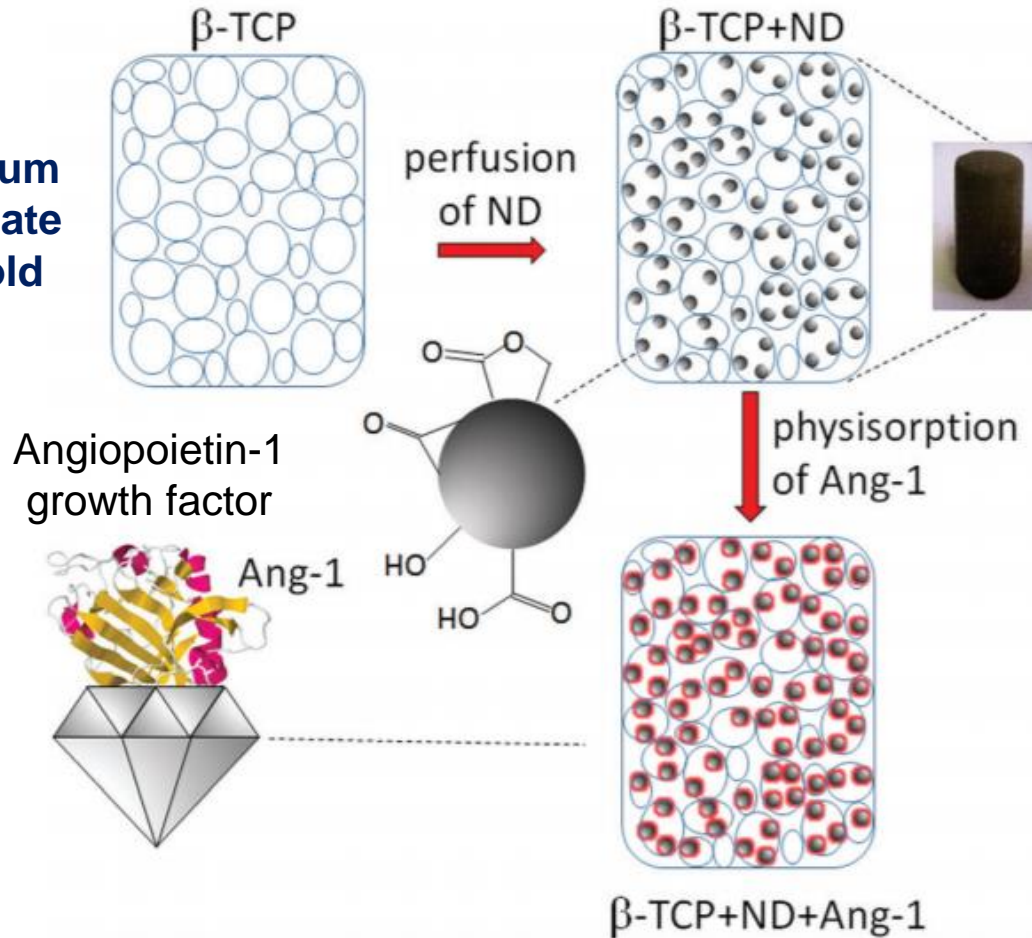
root canal tooth implant:

clinical studies under
progress

Lee et al., ACS Nano 2015

clinically approved

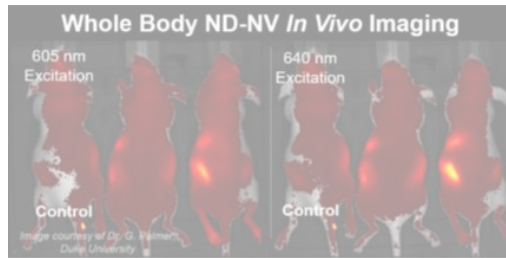
tricalcium phosphate scaffold



better vascularization and bone formation *in vivo* (sheep model)

Imaging

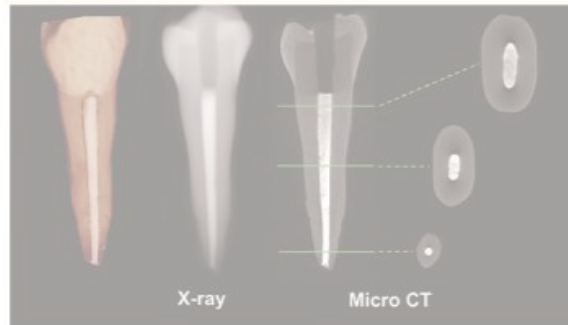
Cell tracking
MRI contrast agent



Biocompatibility
Surface chemistry
Size
Color centers

Implants

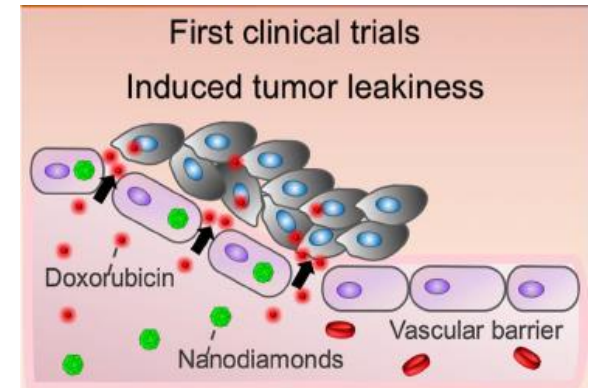
Canal therapy
Bone engineering



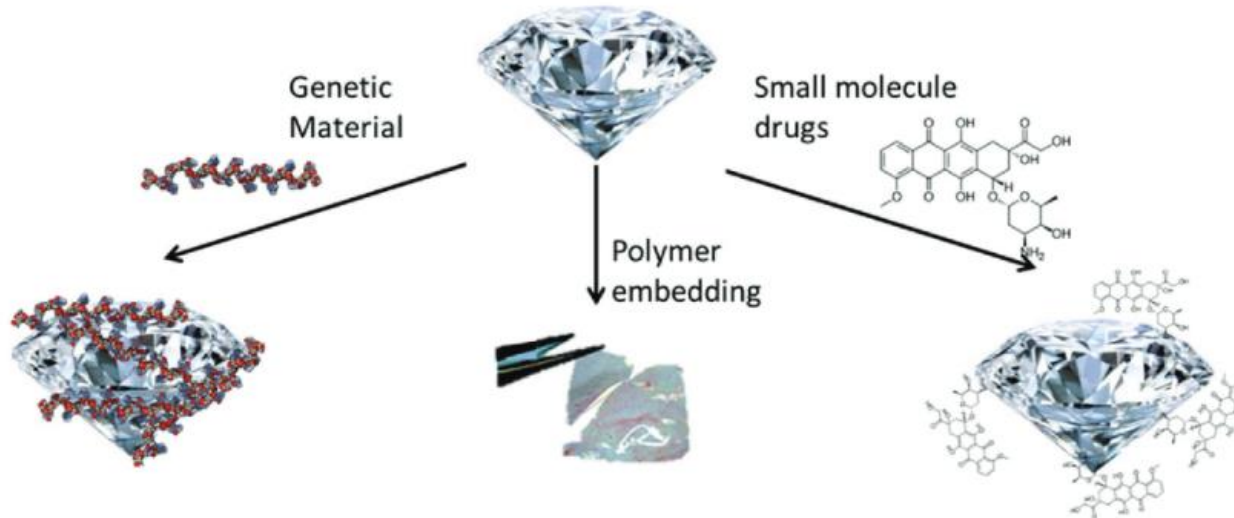
Biocompatibility
Surface chemistry
Mechanical properties

Drug delivery

Cocktail of drugs



Biocompatibility
Surface chemistry
Size



- microRNA, protamine sulfate and cyanine(1)
- siRNA(2)



Mouse: esophageal tumors,

- morphogenetic proteins on DND in polymer scaffold(3)
- antibiotic (4)



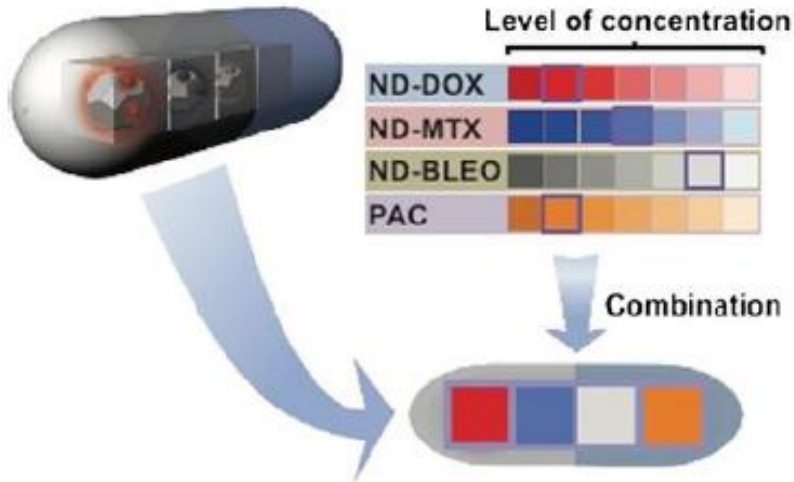
Mouse: bone regeneration
Human: tooth canal

- Doxorubicin (5)
- Paclitaxel (6)
- DOX+folic acid(7)
- Epirubicin(8)
- Alendronate(9)



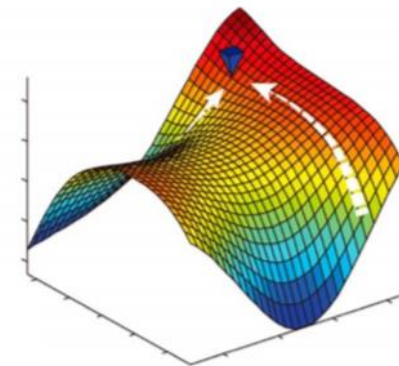
Mouse: liver, mammary cancer, lung metastasis
Rat: brain tumor, bone

doxorubicin bleomycin mitoxantrone paclitaxel

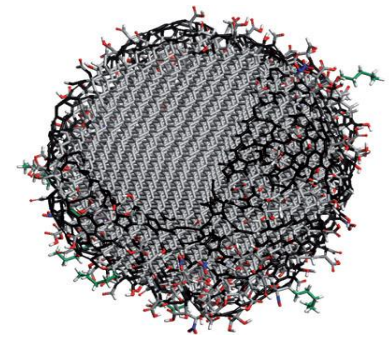


Three different breast cancer cell lines

combinations of drugs in different concentrations



Global optimum of ND-drug cocktail ratios



Combination of physical & chemical properties

Biocompatibility, tunable size, surface chemistry, color centers, mechanical prop.

 **broad field of bioapplications**

Imaging

photostable FND

in vitro and *in vivo* tracking

long term tracking

MRI contrast agents

Implants

root canal tooth implant
(clinical studies in progress)

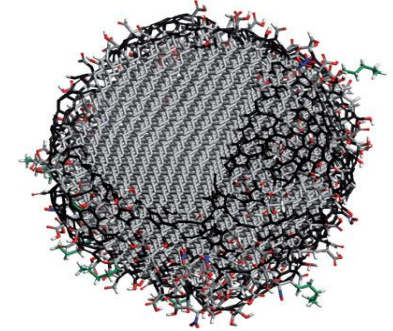
bone tissue engineering

Delivery

genetic materials

molecule drugs

drug combination



Imaging

size down to 10 nm

deep tissue imaging

magnetic modulation

NIR (SiV, EuV/ dyes)

photoacoustic imaging

coupling with hyperthermia

MRI contrast agents (T1 and T2)

Implants

results of clinical studies

mixtures of growth factors

Delivery

use for humans

adapt targeting

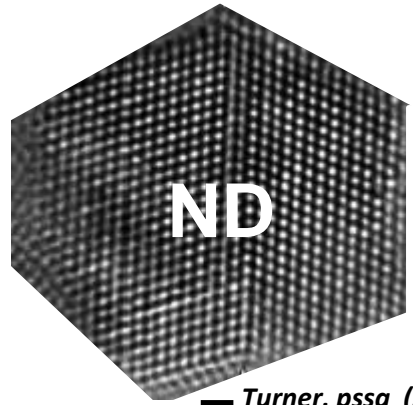
limit aggregation (coating)

Translation to clinics

biodistribution/pharmacokinetics

more interdisciplinary research

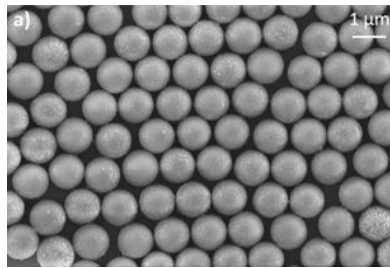
Surface modifications



ND

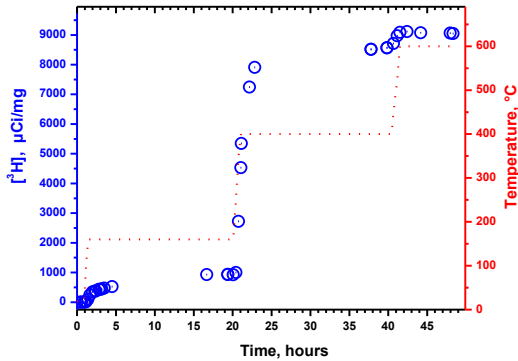
Turner, pssa (2013)

Diamond core shells



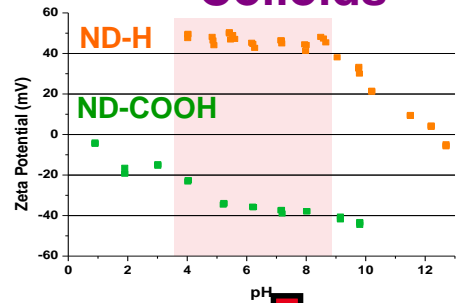
Venerosy et al Diam. Relat. Mater. 2018

Isotopic labelling

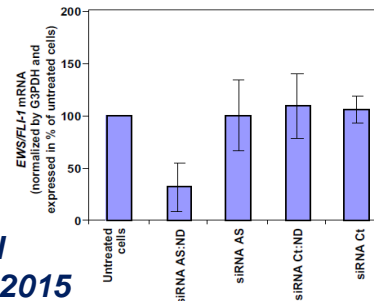


Nehlig et al Nanoscale 2019

Colloids

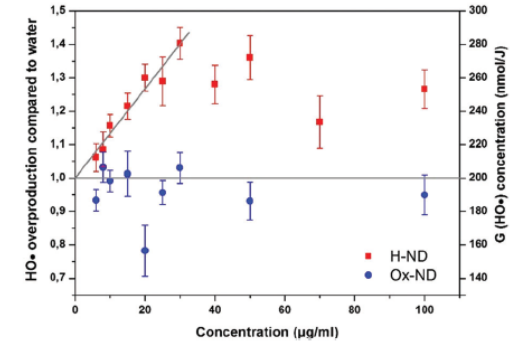


siRNA delivery



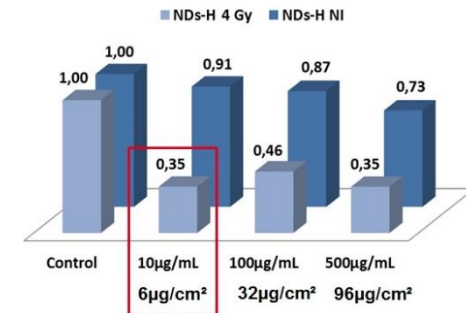
Bertrand et al Biomaterials 2015

Radicals & electrons



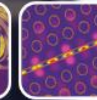
Kurzyp et al Chem. Comm. 2017

Radiosensitisation



Grall et al Biomaterials 2015

THANK YOU FOR YOUR ATTENTION!



Diamond Sensors Laboratory



NANODIAMONDS

Advanced Material Analysis, Properties
and Applications

Edited by
Jean-Charles Arnault

Micro & Nano Technologies Series