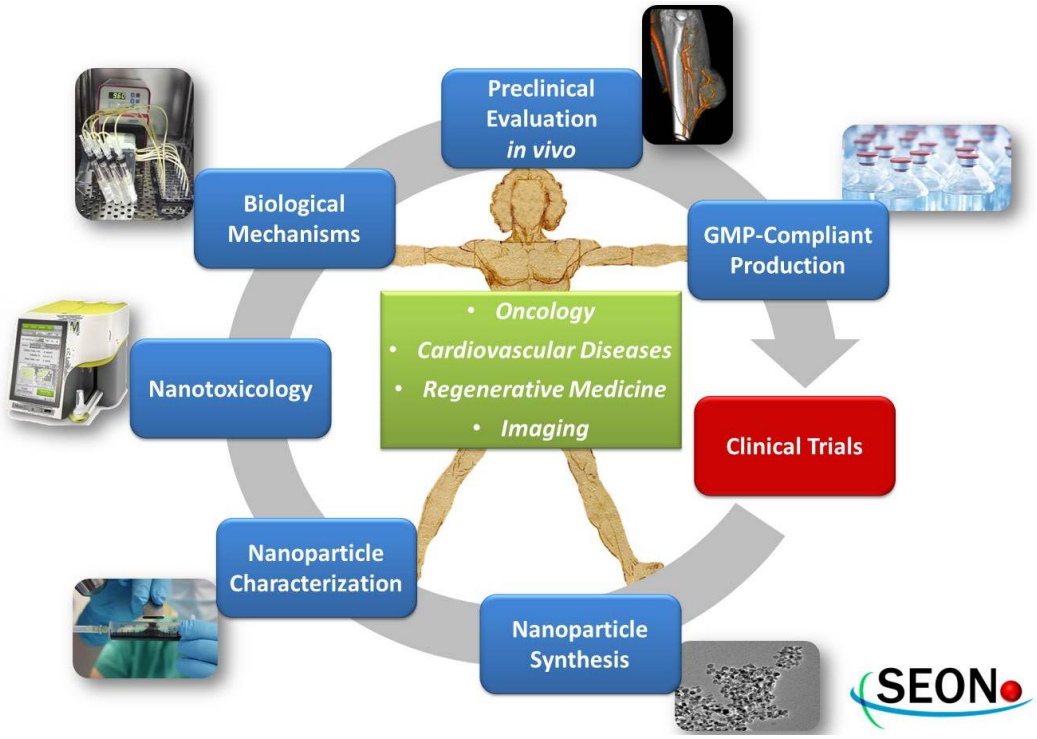
Christoph Alexiou*

Biomedical applications using magnetic nanoparticles-the SEON-concept



Abstract: A multitude of different applications for magnetic nanoparticles were already investigated. Most prominent are drug delivery, imaging and several diagnostic *in-vitro* methods. To implement nanotechnological applications into clinics it is advantageous to cover all development stages starting from synthesis over characterization to the production of respective material under quality controlled conditions (cGMP)

Keywords: SPIONS, Nanomedicine, Drug Delivery, Imaging.

https://doi.org/10.1515/cdbme-2017-0165

1 Introduction

Nanotechnology has caught much attention during the last decades and has revolutionized the energy and electronics sector where it has already reached commercial scales. Moreover, nanoparticles are suitable for many different applications in medicine, concerning diagnostics, imaging and drug delivery. Especially magnetic iron oxide nanoparticles are promising due to their broad spectrum of deployments. Due to their intrinsic properties of certain magnetic susceptibility, they are ideal for contrast enhancement of T2 weighted images in MRI. Another important example is drug delivery by external magnetic forces and thereby utilizing the ability of superparamagnetic nanoparticles to get attracted only if an external magnetic field is applied to the region of interest. To translate basic

***Corresponding author: Christoph Alexiou:** ENT-Department, Section of Experimental Oncology & Nanomedicine (SEON), Else Kröner-Fresenius-Stiftung Professorship for Nanomedicine, University Hospital Erlangen, Glueckstr.10a, 91054 Erlangen, Germany.

findings into clinical trials several requirements such as detailed synthesis and characterization of the nanoparticles, nanotoxicological testings, *ex vivo* models to simulate *in vivo* conditions for appropriate adjustment of the necessary parameters and pre-clinical animal studies have to be addressed. These results are of pivotal importance to start with respective GMP production and approval, which is essential for bring these products into clinical trials.

SEON (Section of Experimental Oncology and Nanomedicine) addresses these issues with a special focus on drug delivery in oncology [1] and further promising potential applications for cardiovascular diseases [2], regenerative medicine [3] and imaging [4]. The overall aim is the translation of promising preclinical results into clinical trials and the respective steps necessary to gain these ambitious objects.

2 Ambition

The Section of Experimental Oncology and Nanomedicine (SEON) has been active in field of cancer therapy since 1999. The major aim of SEON is to bring magnetic drug targeting (MDT) into the clinics as an enduring alternative for classical therapeutic regimes for cancer treatment (see **Figure 1**). Of central importance is the development of reproducible superparamagnetic iron oxide nanoparticle synthesis suitable for GMP-conform production that can be scaled up to industry levels. To achieve this, the particles have to be evaluated as much as possible by physicochemical, *in vitro* and *in vivo* methods for important features such as stability, drug load and release, magnetic properties, toxicity or biocompatibility, effectivity and many more. But for a successful new treatment concept such as MDT, a suitable clinical application environment is also crucial. This includes the development of electromagnets that can be implemented into a radiological intervention suite and the evaluation of visualization methods for superparamagnetic iron oxide nanoparticles (SPIONs) in the tumor area after the application procedure. Therefore, the SEON-labs comprise a chemical subunit for iron oxide nanoparticle synthesis and characterization, a preclinical biological subunit dealing with nanotoxicological issues as well as the biophysical mechanisms of MDT and developing applicable methods for the clinical practice of MDT. Finally, SEON has built up a GMP-facility in the pharmaceutical department of the University Hospital Erlangen which is necessary to produce nanoparticles in a quality needed to apply for clinical studies.

The nanoparticle development circle is also important for further biomedical applications of SPIONs. In the last years, in our group new promising approaches for biomedical applications arose. As an example, for tissue engineering SPIONs can be taken up by endothelial cells to make them magnetically steerable. Using special magnetic arrangements, those SPIONs-labelled cells can form vocal folds as a future supplement for cancer patients. Another very promising application is MRI. SPIONs which were developed in our lab show extra ordinary properties concerning biocompatibility in comparison to once commercially available particle-based MRI-contrast agents. This could be especially important for clinical implementation as the discussion about adverse side effects for gadolinium based contrast agents is currently very prominent. Even the concept of magnetic drug targeting can reach further selectivity levels when it is combined with additional mechanisms of efficacy. Photodynamic therapy is a treatment approach of superficial tumors by applying light after the administration of photosensitive substances [5]. To avoid adverse side effects due to the systemic distribution of those compounds, MDT can make this concept much more selective. The same applies for combining neutron capture therapy, the principle of generating massive radiation damages after weak exciting neutron irradiation, as boron containing substances can be deposited by magnetic nanomaterials and external magnetic fields [6].

3 Conclusion

The SEON-concept is dedicated to bring MDT and several other promising biomedical approaches in combination with SPIONs into the clinic for more efficient treatments and diagnostics with significantly reduced side-effects. The central point is the combination of chemical, pharmaceutical, physical, biological, nanotoxicological and medical expertise within one group. The short communication distance and direct feedback loops between the different subunits are created in order to accelerate the translation of SPIONS related applications into a clinically relevant treatment option improving the outcomes of respective patients, as well as their quality of life.

Author's Statement

Research funding: The author gratefully appreciate the support of this work by DFG (AL552/5-2), Cluster of Excellence Engineering of Advanced Materials(EAM), Margarete Ammon Stiftung and the Bavarian State Ministry of the Environment and Consumer Protection (74a- U8793-2012/7–35), the EU project FP7-NMP-2012-LARGE-6-309820 ‘‘NanoAthero”. Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent is

not applicable. Ethical approval: The conducted research is not related to either human or animals use.

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