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Review

Public–private partnerships in translational medicine: Concepts and practical examples

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ABSTRACT

The way forward in multidisciplinary research according to former NIH's director Elias Zerhouni is to engage in predictive, personalized, preemptive and participatory medicine. For the creation of the optimal innovation climate that would allow for such a strategy, public–private partnerships have been widely proposed as an important instrument.

Public–private partnerships have become an important instrument to expedite translational research in medicine. The Netherlands have initiated three large public–private partnerships in the life sciences and health area to facilitate the translation of valuable basic scientific concepts to new products and services in medicine. The focus of these partnerships has been on drug development, improved diagnosis and regenerative medicine. The Dutch model of public–private partnership forms the blueprint of a much larger European initiative called EATRIS [1]. This paper will provide practical examples of public–private partnerships initiated to expedite the translation of new technology for drug development towards the clinic. Three specific technologies are in focus: companion diagnostics using nuclear medicine, the use of ultra high field MRI to generate sensitive surrogate endpoints based on endogenous contrast, and MRI guidance for High Intensity Focused Ultrasound mediated drug delivery.

Contents

1. Introduction

Innovation in healthcare is clearly a multidisciplinary process and the road to success may be extremely long and windy. Cooperation between academia, industry and health care providers is vital. This is driving the unique Dutch infrastructure of public–private partnerships in the life sciences sector in which academia and industry work together to translate basic knowledge into healthcare products and services – essentially, to innovate together in an open way.

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It is a general misconception that public–private partnerships equal contract research for providing services. Obviously, outsourcing of industrial R&D to public research institutions (universities and or academic medical centers) is not a totally new concept. The quintessence of a successful public–private partnership lies in its integration of academic and industrial research. Key elements are a bidirectional exchange of ideas and expertise and sharing of high-end facilities and equipment to accelerate translation of valuable basic scientific insights in new products. Innovation is quite often a non-linear process quite different from the traditional concept in which academia generates new basic insights that can be handed over to industry to be developed in products.

Obviously, as translational research deals with bench-to-bed side and bed-to-bench side research, and therefore both basic and applied sciences can be found in academia as well as industry, a continuous exchange of ideas between scientists in academia and industrial R&D groups is essential to realize successful translational medicine [1]. In addition, to increase public–private interactions to achieve efficient translation in modern medicine, the regulatory environment will have to be adapted as well to accommodate new approaches in the drug development process.

1.1. Public–private partnerships in The Netherlands: Hotbed for interdisciplinary research

Three leading Technology Top Institute's (TTI) represent the majority of the public–private landscape for the life sciences in the Netherlands: Top Institute Pharma (TI Pharma, http://www.tipharma.com), the Center for Translational Molecular Medicine (CTMM, http://www.ctmm.nl) and the BioMedical Materials program (BMM, http://www.bmm-program.nl) . The three institutes jointly focus on complementary application areas in medicine: drug discovery and development, diagnosis and imaging of biomarkers (including image guidance and monitoring of drug delivery) and regenerative medicine and stem cell therapies. The focus of these initiatives is on pre-commercial R&D activities aimed at the expedited translation of new scientific findings into clinical proof of concept studies (up to Phase I, IIA trials). The actual agent development and extensive clinical testing (beyond phase IIA) and approval procedures are outside the scope of these public–private consortia active in the Dutch life sciences.

The research funding in the TTI's is composed of 50% governmental contributions matched by 25% funding by public partners and 25% by private partners (large industry, SME's). The private contributions are equally split in an *in cash* and *in kind* contribution, whereas public matching is in kind only. The consortia are being supported by the most prominent charity foundations in the Netherlands and include patient advocacy groups as well, an often overlooked aspect of building a large coalition for the translation of basic sciences into valuable solutions, services and products in healthcare. In this context one should rather speak from public–private-patient partnerships.

The funding is distributed (competitively) by the TTI's among consortia of private and public partners that represent the best talent and conditions for a particular disease related challenge. Unbiased, international peer review and a final assessment by a (non-Dutch) International Scientific Advisory Board constitute the quality assessment and selection process. Scientific quality is key, but more than in basic science proposals, economic and clinical potential and impact jointly carry a similar weight as scientific excellence.

To overcome some of the major challenges that this type of partnerships create, an extensive framework of clear boundary conditions has been created for the execution of the research in a "PPP" context. An important aspect and often an impediment for the implementation of private partnerships are intellectual property rights. Negotiations over patent and license rights have a tendency to overcomplicate potential partnerships. The Dutch model has been based on a uniform agreement that addresses the basic rules for private partnerships of clear obligations and fair rewards. In essence, back ground IP is protected from commercial use but will be shared for research purposes, whereas a fair remuneration for academic partners is guaranteed in case foreground IP is generated. Moreover, intellectual ownership will reside with the original inventor(s), whereas economic ownership is shared with all contributing partners in the consortia.

Training and education is an important aspect of implementing an efficient intellectual property policy in the public–private setting. Academic researchers will have to be trained to understand the role and value of intellectual property for the translational process, academic tech transfer offices (TTO's) have to be coached in the assessment of the proper value of IP generated. Industry has to be aware that sharing value of IP generated with academia may feed into more long term collaborative relationships that in the end may be much more effective and rewarding for effective innovation than short term contract research relationships. Another important aspect of IP in a multi-disciplinary context is the different value IP has for different disciplines. For drug development a single patent may be absolutely crucial for the value chain of a certain development cycle, whereas in the device industry products may embed a broad spectrum of different patents for which cross licensing is much more common and the actual value of a single patent is limited.

Besides being challenging, the advantages of joining forces between different scientific and industrial cultures can be extremely rewarding as well. The focus areas of the three TTI's in the Netherlands are separate with different dynamics. Where the entire pipeline to develop and register a new drug has become excessively long and costly, for medical devices, biotechnology and in vitro-assays a much more expeditious time to market is not uncommon. For regenerative medicine, the regulatory framework is partly still work in progress. However, there are ample opportunities for cross-fertilization between these different disciplines. Companion diagnostics will provide new imaging and in-vitro assays that will contribute to the assessment of drug targeting efficacy and introduce new surrogate endpoints that may short circuit lengthy clinical trial procedures. Image guidance will create a new window of opportunity to develop new strategies of drug delivery and other forms of therapeutic interventions such as radio- and proton therapy, chemo- (TACE) and radio-embolization, brachy therapy, radiofrequency and HIFU ablation. In this context molecular imaging application and the development of tracers that link drug development with image based validation and efficacy biomarkers have become an important new field based on synergies in the drug development and imaging communities.

In the following sections three examples are described where a Dutch public–private partnership approach brings together the best partners in industry (national/global) and Dutch universities to improve diagnosis and therapy. These three examples provide illustrations of actual public–private partnerships in pre-commercial R&D to facilitate the clinical introduction of new therapies exploiting diagnostic imaging technologies.

2. Example 1: molecular imaging and tracers

One of the most important unmet needs in the development and use of new drugs are new in vitro or in vivo biomarkers that can be used as (surrogate) endpoints to assess therapeutic effects. Imaging, combining high resolution spatial information with specific functional and molecular information, is making important inroads in producing such new biomarkers. Molecular imaging is of value for sensitive visualization and quantification of critical disease targets and targeting molecules – either drug candidates or diagnostic agents – at high resolution [2]. As such, molecular imaging is of high utility for initial diagnosis and prognosis, treatment selection and guidance, outcome monitoring, and new drug development.

Ample literature has described the use of imaging in drug development [3–5] Key in molecular imaging is the exploitation of critical biomarkers involved in pathogenic processes, and the development of "disease-specific contrast agents", herein collectively called "tracers". Some biomarkers need association with a tracer for visualization, while others do not (e.g. oxy/deoxyhaemoglobin using functional magnetic resonance imaging (fMRI), changes in phospholipid metabolism in ^{31}P magnetic resonance spectroscopy (MRS)). In addition, validated methods are needed to visualize the biomarkers (semi)quantitatively by an imaging modality and to process and interpret images. Tracers, which can be used in nuclear (positron emission tomography (PET)), radiological (MRI & ultrasound (US)) and/or optical procedures, enable visualization and quantification of critical disease targets and molecular processes, or serve to track (targeted) drugs (e.g. monoclonal antibodies, peptides, small molecules etc.), carrier systems (e.g. liposomes) or cells in vivo. In addition, molecular imaging can be used to assess the effect of (unlabeled) pharmaceuticals on critical disease processes, which are imaged with the proper imaging procedures and tracers. For these applications, PET, US, Ultra High Field MRI and even (near infrared) optical imaging methods are considered to be the most powerful. By using molecular imaging strategies for initial diagnosis, for treatment selection and guidance as well as for response monitoring, possibilities arise for real "personalized medicine" as illustrated in Fig. 1. Two distinct new modalities play an important role in the translation of new therapeutic options into the clinic: PET (tracer) Imaging and Ultra High Field MRI.

3. PET imaging

It is anticipated that further progress in healthcare will be obtained by identification of molecular processes and targets involved in the development and progression of disease, thereby enabling personalized targeted treatment at the molecular level. Positron emission tomography (PET) is the technique of choice for imaging molecular processes and targets at a *picomolar* level. PET plays a key role in rapid diagnosis of disease, efficient development of novel (targeted) drugs and therapies, and in the individualization of treatment by patient selection and monitoring response to therapy.

One of the first tracers used in PET was [^{18}F]-fluoro-2-deoxy-D-glucose (^{18}FDG), a glucose analogue, which allows for mapping (and measuring) glucose metabolism. At present, this tracer is used in more than 90% of all PET imaging procedures with applications in e.g. oncology, neurology, immunology and cardiology.

The starting point in tracer development is the production of positron emitters such as ^{11}C, ^{13}N, ^{15}O, ^{68}Ga, ^{18}F, ^{124}I, and ^{89}Zr. For a positron emitter to be suitable for tracer development, it has to fulfill several requirements. The positron emitter should have appropriate decay characteristics for optimal resolution and quantitative accuracy, and it should allow for easy, efficient, and stable coupling to the parent compound (ligand) of interest. Maintenance of *in vivo* binding and biodistribution characteristics of the parent compound is imperative. Moreover, the physical half-life ($t_{1/2}$) of the positron emitter should be compatible with the time needed for a tracer to achieve optimal biodistribution. Using this criterion short-lived positron emitters like ^{11}C ($t_{1/2}=20$ min) and ^{18}F ($t_{1/2}=110$ min) might be suitable for labeling of small molecules with fast kinetics like tyrosine kinase inhibitors (TKIs), whilst long-lived positron emitters like ^{89}Zr ($t_{1/2}=78$ h) and ^{124}I ($t_{1/2}=100$ h) are ideal for larger molecules with slow kinetics, such as intact monoclonal antibodies (mAbs). The choice of positron emitter to be used also has consequences for logistics. Whilst ^{11}C-tracers can only be used at the site of production, ^{18}F-tracers can be distributed over a 3 h distance, and ^{89}Zr- and ^{124}I-tracers can and are distributed worldwide. In addition to ^{18}FDG, a battery of tracers can be produced routinely for PET imaging of a variety of pathological processes. Some tracers provide biological

Fig. 1. PET tracers can be used for tumor detection (step 1), for confirmation of selective tumor targeting by a specific targeted drug (step 3) and for early assessment of therapy response (step 5): "The right treatment, at the right time for the right patient." (PET images obtained from Dr. K Muylle and Prof P Flamen, Jules Bordet Institute, Brussels).

information on tissue metabolism or microenvironment and are particularly suitable in oncology, e.g. ^{18}F-FLT (cell proliferation), ^{11}C-methionine (amino acid transport), ^{18}F-methylcholine (membrane synthesis), $^{15}O_2$ (oxygen metabolism), $H_2^{15}O$ (tissue perfusion), and ^{18}F-MISO, ^{18}F-AZA and ^{18}F-HX4 (oxygenation). Others are of interest as receptor binding ligands in neurological diseases, like ^{11}C-flumazenil ($GABA_A$ ligand, epilepsy), ^{11}C-PIB (protein aggregates, so-called plaques in Alzheimer's disease), ^{11}C-PK11195 (inflammation), ^{18}F-FDDNP (protein aggregates, plaques and tangles in Alzheimer's disease), ^{11}C-raclopride (D_2 ligand, movement disorders, schizophrenia), ^{18}F-fallypride (extrastriatal D_2 receptor ligand, attention deficit), ^{11}C-R116301 (NK1 ligand, depression),^{11}C-WAY100635 and ^{18}F-MPPF ($5HT_{1A}$ ligand, depression, anxiety), ^{11}C-R107474 (α2 receptor antagonist, depression), ^{11}C-DASB (seretonine transporter, depression), ^{18}F-FP-β-CIT (dopamine transporter, Parkinson's disease), ^{11}C-deprenyl (MAO-B ligand, Parkinson's disease), and ^{11}C-verapamil (P-gp ligand, drug resistance). Within the private-public consortia in the Netherlands, several novel tracers are under development for imaging hypoxia, amyloid-β, glutamate neurotransmission system, transglutaminases, muscarin acethylcholine receptors, seretonin receptors, folate receptor, p-glycoprotein (e.g. ^{11}C-laniquidar), the peripheral translocator proteins, etc.

Increased knowledge of the targets involved in critical disease processes has boosted the design of cutting edge pharmaceuticals, ranging from small molecules like tyrosine kinase inhibitors (TKIs) to large biotech products like monoclonal antibodies (mAbs). The yearly sales of TKIs is 16 billion dollars, of mAbs 30 billion dollars. Despite this boost, the number of annual new drug approvals has remained constant during the past decade. Among the potential roadblocks in new drug development are increased costs, which particularly result from increased drug evaluation processes including costly clinical trials and increasing regulatory demands. It is clear that drug failure at a late stage in the clinical development (phase III trials) is the worst case scenario for pharmaceutical companies. For this reason, many companies include potential labeling with a positron emitter in their drug development program. This strategy enables in vivo tracking of the drug by PET upon administration to a patient in early stage clinical trials (Phase 0 - microdosing, I and II). Quantitative information can be obtained about e.g. pharmacokinetics and biodistribution, disease targeting, normal tissue accumulation, excretion routes, receptor occupancy, biological half-life in tissue, inter-patient variability, and biodistribution during combination therapy. Based on its test-retest accuracy, PET can provide this information efficiently with fewer patients in clinical trials. As such, it may contribute to identification of high potential drugs with a broad therapeutic window, improved drug dosing schedules, identification of patient groups with best chance of benefit from drug treatment, and efficient use of new drugs in combination therapy.

Among the exciting novel tracers which are explored within the public–private context are ^{11}C-docetaxel and the TKIs ^{11}C-erlotinib, and ^{11}C-sorafenib (so-called TKI-PET) [6]. In addition, the researchers involved introduced universal radiochemistry, enabling tracking of mAbs (so-called immuno-PET) and other biotech products *in vivo*. To this end, solutions have been developed for large scale production of the positron emitters ^{89}Zr and ^{124}I, and for their efficient and stable coupling to mAbs. ^{89}Zr is coupled indirectly via a chelate and is particularly suitable in combination with internalizing mAbs, while ^{124}I can be coupled directly and is used in combination with non-internalizing mAbs. Immuno-PET can be used in cancer staging, for the improvement and tailoring of therapy with existing MAbs (Fig. 2), and in the efficient development of novel mAbs or non-traditional mAb-like scaffolds [7,8] At present, immuno-PET technology is disseminated worldwide and several leading antibody companies are implementing this technology in their drug development program (e.g. Genentech) [9] In addition, several Dutch academic centers are building extensive research programs on this technology.

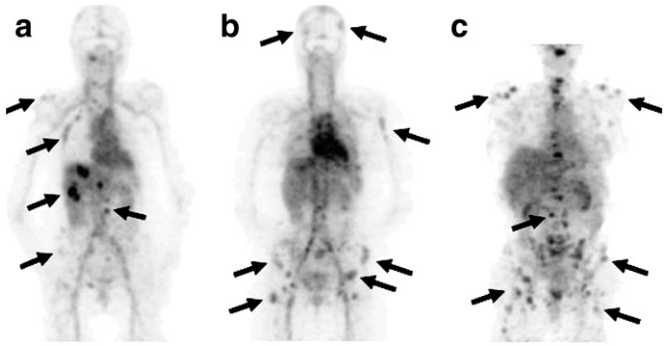

Fig. 2. Examples of ^{89}Zr-trastuzumab uptake 5 days p.i. in a patient with liver and bone metastases (a) and two patients with multiple bone metastases (b + c). A number of lesions have been specifically indicated by the arrows (from Dijkers et al. [7]).

This type of imaging clearly demonstrates the added value of public–private interaction by combining academic expertise in the field of clinical (PET)imaging and tracer development combined with drug development in private companies with a clear need of early detection of drug efficacy in a clinical setting. In 2011 three academic centers in the Netherlands ("Dutch Imaging Hub") entered a R&D agreement with the Swiss company Roche to accelerate drug development by means of (companion) molecular imaging technology. (http://www.habg.nl/news/item/44/Dutch+Imaging+Hub+accelerates+development+of+medicines)

4. Example 2: ultra high field MRI

Due to its non-invasive nature and lack of ionizing radiation, MRI is the modality of choice for anatomical and functional imaging, early detection of pathology or long term follow up of therapy response. Within public–private partnerships in The Netherlands, several applications are under development in translational neurology for early diagnosis of neurodegenerative disease (Alzheimer [10], vascular dementia), multiple sclerosis [11], epilepsy, brain neoplasm and stroke, as well as applications outside the brain addressing oncology (breast [12] and prostate cancer), diabetes (liver metabolism), cardio-vascular diseases (carotid atherosclerosis, peripheral and coronary artery disease) and rheumatoid arthritis. High field contributes to more signal and concomitantly better spatial resolution and/or shorter scan times. Even more important is the substantially altered potential for very specific contrast generation based on *intrinsic* tissue characteristics. Where PET provides very high sensitivity to detect very low concentrations of tracer molecules and ultrasound derives its strength from the capability to study dynamic processes, MRI excels in spatial resolution and detailed functional information directly derived from the (pathological) tissue itself. This creates an important opportunity to study *in vivo* biology in human subjects without the need for agents that may interfere with the biological processes under examination or that may be harmful to the patients. For neurological disorders (degeneration, depression) there is a clear need for early assessment of the onset of abnormal phenotypes of the brain. Detailed characterization of substructures of the hippocampus, cortical layer determination, abnormalities of subtle vascular structures, neuro-transmitter metabolism (glutamate, GABA) [13,14] and many other examples have proven to depend on ultra high field MRI protocols. Even more so, from the current data of 7 T it becomes clear that high field can progressively improve tissue characterization based on new contrast mechanisms. These new insights will have a major impact on biomarker development (surrogate endpoints of drug trials), the *in vivo* monitoring of regenerative medicine and drug response monitoring. All these techniques will also ease the faster translation of new fundamental insights in the clinical setting.

As shown in Fig. 3, 7 T brain imaging is already in use to assess neurological disorders, illustrated by the direct visualization and the

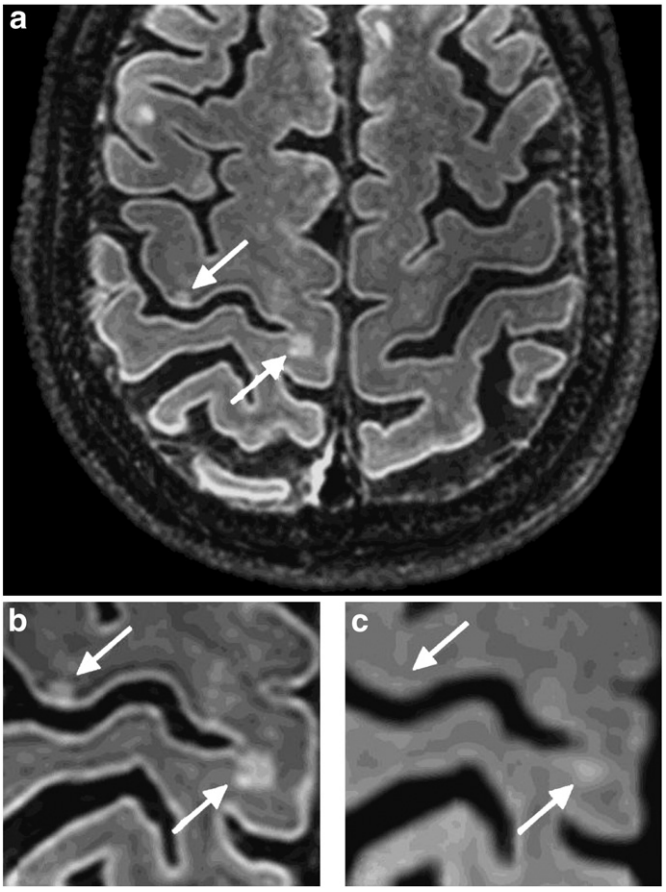

Fig. 3. Detection of cortical lesions in MS. Patient with primary progressive multiple sclerosis (MS, EDSS 6.0). A 7.0 Tesla MRI scan was performed for detection of possible cortical lesions. (a) Axial overview and (b) zoomed-in image of a high parietal cortical MS lesion (right arrow) on axial 7.0 Tesla 3D-FLAIR sequence. The 3 T (c) image in retrospect did show the lesion as well, but the increased conspicuity of the lesion at 7 T is clearly demonstrating the clinical potential of 7 T neuro-MRI.

detection of small (cortical) MR lesions that otherwise would not be conspicuous at lower (3 T) MRI field strengths.

The introduction of ultra high resolution imaging of soft tissue in academic centers will provide new surrogate endpoints that may substantially improve the early assessment of drug efficacy in patients. Clearly, in the end this will not obviate the need for many larger clinical trials. But as clinical trial design will allow for more adaptive protocols, high definition imaging may become an important instrument to expedite the development process.

5. Example 3: image guided therapy (*surgery without incisions*)

There is a growing interest in minimally invasive image-guided therapy, the idea being to cure disease while doing as little harm as possible to the patient. Medical imaging systems play an important role in minimally invasive procedures, providing images of patients before, during and after the procedure in order to plan, guide and evaluate the results of therapy. Such methods result in fewer complications, fewer and smaller scars, are more patient friendly and may result in substantial cost containment. In addition, patients recover more quickly and leave the hospital sooner, leading to lower healthcare costs. Between 1953 and 1979 a *silent revolution* has taken place by pioneering work of Seldinger, Dotter, Gruentzig and Palmaz to safely insert catheters and perform angioplasties and stent deliveries rather than surgical removal of artery obstructing plaques. In this case one may describe this as a major paradigm shift regarding therapy of vascular pathologies. A similar shift is about to happen in cancer treatment, where a broad spectrum of new approaches is being investigated. One of those new techniques, currently being explored in a public–private partnership between industrial and academic imaging and drug development experts, is image guided High Intensity Focused Ultrasound for tissue ablation and local drug delivery.

It is possible to focus ultrasound and project it into a patient in such a way that the acoustic energy ends up predominantly in one location – the focal point. At the focal point, local heating of the tissue will occur, which can be used to kill tumor cells. This process is called thermal ablation. The possibility of locally heating tissue without doing harm to surrounding tissue opens a pathway towards new therapeutic strategies with improved reliability and less associated trauma, leading to improved efficacy, reduced periods of hospitalization, reduced treatment costs and improved quality of life.

High Intensity Focused Ultrasound (HIFU) is the only known technique capable of completely non-invasive controlled heating deep inside the human body. Up until now it has been used primarily for the treatment of uterine fibroids, guided by ultrasound imaging. However, when using ultrasound guidance, 3-dimensional information is frequently lacking and accurate temperature mapping is not possible. Magnetic Resonance Imaging (MRI) seems better suited for HIFU guidance than ultrasound, as it allows continuous imaging of the tumor and the surrounding healthy tissue. In addition, MRI can be used to acquire temperature maps inside the patient. Such maps can be used to control the heating procedure using feedback control methods to make sure the tumor is heated adequately. Furthermore, MRI imaging techniques can be used afterwards to check treatment efficacy. For non-malignant disease (uterine fibroids), MR guided HIFU already has taken its position in routine healthcare as an alternative of the current embolisation treatments. For malignancies, several technological challenges have to be dealt with before routine clinical application of thermal ablation for management of breast cancer and liver metastases can be considered. An important problem is making sure that no residual viable tumor cells are present after ablation. So far, HIFU ablation has been performed using a point-by-point ablation method, which inherently does not cover the whole treatment volume with the same thermal dose. The long treatment duration is considered problematic since patients need to remain immobilized throughout the whole procedure. This further complicates ablation of malignant tumors in a moving organ like the liver which requires additional important technological developments and innovations. The system must be adapted to take the motion of the liver into account, both with respect to positioning of the focal point, as well as to correcting for motion artifacts in rapid temperature mapping. The higher blood flow and perfusion rates in the liver, as well as the presence of the ribs, require further modifications of the platform, specifically with regard to managing the spatiotemporal ultrasound power deposition. Furthermore, there is a lack of accurate and reliable imaging techniques for per- and post-interventional assessment of therapy response and treatment results.

As a next step, site-targeted delivery of small-molecular-weight drug molecules and biologicals is increasingly recognized as the key to increasing the therapeutic index (i.e. the efficacy/toxicity ratio). Temperature-responsive drug delivery vehicles (e.g. temperature-sensitive liposomes) that release their payload in response to a local temperature increase offer the potential to improve therapeutic efficacy [15–17]. One way of achieving this local temperature rise and drug release is using the same basic MR guided HIFU technology that is used for direct tissue ablation [18–20]. This application creates exciting opportunities for pharmaceutical companies and researchers to expand applications for existing drugs by altered (and often tunable) pharmacokinetics as well as new opportunities to monitor and validate drug delivery.

The technique using MR-guided High Intensity Focused Ultrasound in combination with temperature-sensitive nanomedicines, may provide new options for the treatment of liver and bone

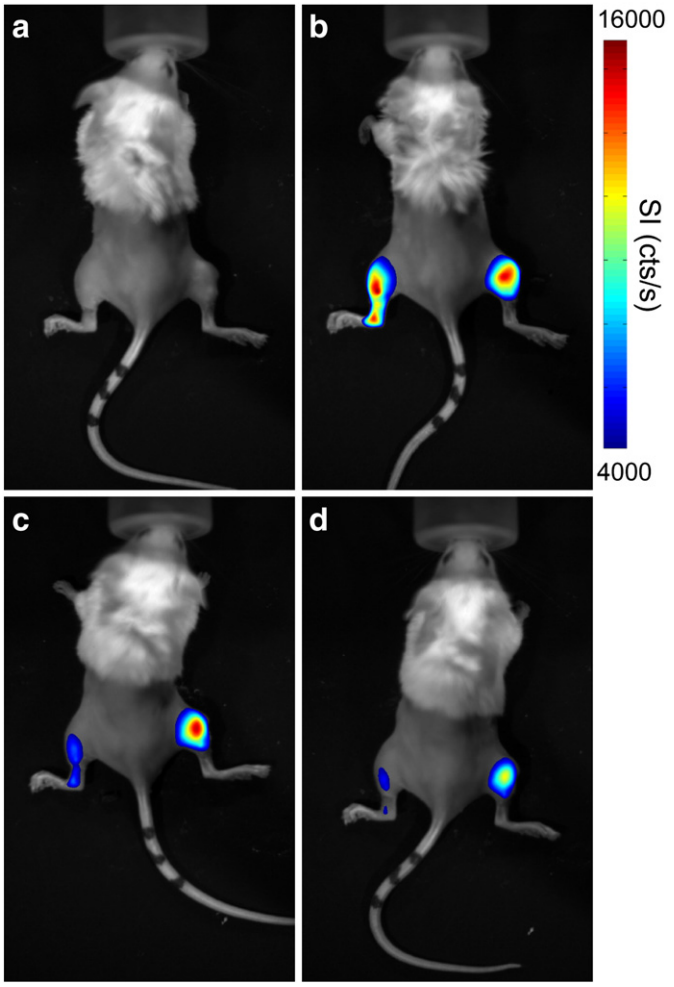

Fig. 4. In vivo Images of optical contrast agent TOTO-3 Fluorescence in Rag-gamma mice with bilateral CMT-93 colon carcinoma. a) Baseline image; b) t = 0 following intratumoral injections of 6 μM of TOTO-3 as a cell-impermeant model drug in 50 μl of Sonovue microbubbles with only the right tumor exposed to ultrasound (1 min sonication at 1.5 MHz using a 6 mm (o.d.) transducer, Pulse Repetition Frequency 1 kHz, Duty Cycle 4%, pressure = 1 MP). c) t = 2 h following injection; d) t = 4 h. The results show ultrasound induced enhanced tumor uptake of the model drug [21].

metastases. MRI provides anatomical information for planning the therapeutic intervention and temperature mapping for local hyperthermia control, as well providing a means of monitoring drug release. In addition to inducing a local temperature raise, the interaction of ultrasound waves with tissue may also enhance extravasation and membrane permeability due to local pressure fluctuations leading to a further increase of drug uptake. This can be further enhanced in the presence of gas filled microbubbles (Fig. 4).

Image guided drug delivery is a clear example of tight collaborative work between academia, device and pharmaceutical industry in which the particular industrial strengths in the Netherlands are being matched with the academic agenda.

5.1. Private–public-patient partnerships: the way forward

The model described provides an example how close collaborations between the major stakeholders can contribute to help overcoming the major innovation challenges in the life sciences and health sector. Some important key factors of success of PPP's are:

- A real integration of public and private R&D (open innovation approaches, exchange of young researchers between academic and industrial laboratories)
- Standard (and fast!) processes for allocation of budgets
- Clear and fair rules on Intellectual Property (non-negotiable!)
- Training of (young) academic researchers in specific aspects of translational research (e.g., working in an IP sensitive environment, overseeing the entire translational pipeline)
- Presence of a basic high quality infrastructure (open access, shared research facilities, an ICT frame work)

For obvious reasons, the rules of engagement of this public–private interaction will evolve with time. But at this point in time, this multi-disciplinary approach where academia and industry define more synergistic ways of in depth collaboration is currently here to stay. And there is no way back.

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