THE COMMERCIALIZATION OF SCIENCE AS AN EMBEDDING PROCESS:
THE CASE OF PET RADIOTRACERS AT UPPSALA UNIVERSITY

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Abstract:

This paper discusses the commercialization of science as an embedding process within a complex network of technical and social resources resources. We rely on a single in-depth case study over the commercialization and de-commercialization of Uppsala PET center in order to identify how PET radiotracers, our focal piece of science, are interfaced with other resources and how they are connected to the three settings of developing, producing and using. We find that the twists and turns in the innovation journey of the PET center depend on deep technical interfaces, problematic mixed interfaces that create conflicts between the involved actors, and shallow organizational interfaces.

Keywords: *Commercialization of science, embedding, network, developing, producing and using*.

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INTRODUCTION

The transformation of scientific results into commercial products or services is a phenomenon which, under the label of “commercialization of science”, has been widely investigated, especially in search of its immediate effects measurable for instance as patents (e.g., Powell & Owen-Smith, 1998) or stressing the linear “spin-out funnel” as a major mode of commercializing science (Clarysse et al., 2005). However, focusing on such direct effects as patents or on spin-off mechanisms neglects several aspects of the complex process of connecting science to industrial or societal needs (Pavitt, 2004; Grandin, Wormbs & Widmalm, 2004). For instance, radiotracers, a key scientific result of PET (Positron Emission Tomography) at Uppsala University were developed from start in close connection with the pharmaceutical industry, and a key contribution to developing some specific type of radiotracers came from hospital physicians and their need of diagnostic tools for oncological endocrinology. Patents were not the focus of the ensuing commercialization episode, nor was the creation of a start-up company planned by the inventors.

As pointed by Perkmann and Walsh (2007), these interaction patterns between academia, on the one hand, and industry or public organizations, on the other hand, are seldom explored in detail by means of thick descriptions. Therefore, the purpose of this paper is to follow in detail these interactions and the resources involved in the commercialization of PET at Uppsala University. After developing the first version of radiotracers, the Uppsala University research group was transformed into an organizational center of its own. But the need of financing its expensive research activities pushed the center closer to industry and healthcare, two important sources of revenues as they needed to use radiotracers and PET scans respectively for drug development and patient diagnosis. As selling radiotracers and PET scans even appeared as a viable business, a private company, GE Healthcare, purchased the entire PET center, including its equipment, personnel and IPRs on specific radiotracers. However, the revenues from selling radiotracers and PET scans were insufficient to turn the newly formed company profitable and GE Healthcare decided to dismantle it. As Uppsala hospital had become strongly dependent on PET diagnostics, the only option for Uppsala University and City Council was to repurchase the former PET center, while IPRs on some radiotracers remained under the company’s control.

In order to make sense of the twists and turns in this complex process, which defies the linearity of the “spin-out funnel” (Clarysse et al., 2005), we approach innovations as an *embedding process* which requires creating connections between the resources found in the three settings of “developing”, “producing” and “using” (Håkansson & Waluszewski, 2007; Ingemansson & Waluszewski, 2009; Baraldi, Gregori & Perna, 2011). More precisely, we penetrate in the interactions between the resources involved by applying the 4 Resources model (Håkansson & Waluszewski, 2002) and analyze their interfaces (Baraldi, Gressetvold & Harrison, 2012). Two specific research questions guiding our investigation are: (1) how are PET radiotracers interfaced with other relevant resources in this embedding process? And (2) how do PET radiotracers get connected with the three settings of developing, producing and using? The paper is organized as follows: first we provide our key theoretical concepts, and then we present our methodology, followed by our case and its analysis.

THEORETICAL CONCEPTS: COMMERCIALIZATION AS THE EMBEDDING OF SCIENCE

Academic science has historically been attributed a key role in driving industrial innovation and economic development (Grandin, Wormbs & Widmalm, 2004). Some industries, such as chemicals and electronic, are even defined as “science-based” due to their dependence for innovations on the cutting-edge science typically found at universities (Pavitt, 1984: 362). While the contribution of academia to industry is undisputed and includes new instruments and methods, the creation of new firms and especially trained graduates (Salter & Martin, 2001), what is instead still widely debated among scholars are the *processes* through which science “contributes to”, and hence the extent to which it “drives” industry. Dating back to the 1940s, a direct and linear sequence has been proposed (e.g., Bush, 1945) going from basic research (performed at universities), which leads automatically to applied research and then to product development and market introduction (performed by companies).

Even if this so called “linear model” (Balconi, Brusoni & Orsenigo, 2010: 5) has been widely criticized due to its oversimplification of the connections between academia and industry (Grandin, Wormbs & Widmalm, 2004), its basic assumptions of science being the driver of innovation and economic growth still persist in the policy recipes that since the 1990s increasingly require universities to undertake measures in order to commercialize or transfer to society their science (Etzkowitz, 2002; Eltzinga, 2004; Wright et al., 2007). Such activities as patenting, licensing and spinning-out companies have consequently received great attention by innovation researchers (e.g., Powell & Owen-Smith, 1998; Zucker, Darby & Armstrong, 2002). However, these activities represent *only a part* of all possible paths and through which academic science can reach utilization in industry and society, and belong namely to the mechanism known as “spin-out funnel” (Clarysse et al., 2005). Reflecting the linear ideal above, this funnel starts from selecting the most “commercially attractive” scientific discoveries and takes them through various steps of refining, including patenting, until they can become incorporated into spin-offs or licensed to established companies (Ibid).

An implicit assumption behind such ideals and models is that the most *cutting-edge* science as soon as it meets a market need, which it can *potentially* satisfy, will have an easy way to success, widespread diffusion, and profits. However, the flow of patents, licenses and spin-offs give an idea only of the most *apparent* and superficial part of the process by which science can be turned into business. Focusing on these apparent elements misses instead what is under the surface of this process and especially the daily “dirty” necessity of finding compromises between the “purity” of science and other interests and all negotiations and interactions that this entails (Latour, 1987). In order to become commercialized the original science needs in fact to be transformed into something else, including “downgrading” the most cutting-edge discoveries, simply because they are too advanced and clash with the established investments and other technologies already in place (Håkansson & Waluszewski, 2007: 6-10). Investigating the commercialization of science requires therefore theoretical and analytical tools capable to focus on the *transformation* of science into “something else” of commercial value: this transformation process is moreover complex, unpredictable and can take many unexpected paths, including reverting the aforementioned linear order (cf. (Dasgupta & David, 1994; Basalla, 1988; Rosenberg, 1994).

In order to become commercialized, science needs in fact to undergo basically the same *innovation process* as any invention that has to find users willing to adopt the new solution. Van de Ven et al. (1999) describe this process as chaotic and resembling a journey in a rugged landscape, with the aggravating factor for science, and especially path-breaking discoveries, that it is typically much farther away from users needs than most other inventions. During this hard and harsh journey separating science from becoming products with users (i.e., an innovation in proper terms, Tidd, Pavitt & Bessant, 2001: 38-9), it will be necessary to *connect* the *tangible and intangible resources* involving *scientists* – who invented the new technology – *producers* – who have to earn money from manufacturing and delivering that solution – and *users* – who are willing to adopt it (Håkansson & Waluszewski, 2007; Ingemansson & Waluszewski, 2009). And it is exactly these complex connections between resources controlled by variegated actors that will transform science, often to such an extent to make it hardly recognizable, when it enters into widespread use: for instance, who would tell that sildenafil, the active substance in a world-known erectile dysfunction drug was originally invented as a remedy against hypertension? Or that the WWW was invented as a document management system for internal use at the CERN research lab?

Therefore, most scientific knowledge is used *indirectly* in the business world, almost hidden, after it has become *embedded* through several connections that have been created with surrounding technologies, actors and organizations (Håkansson & Waluszewski, 2007: 6-7). Consequently, the real problem in commercializing science is not a marketing issue in traditional terms, since patenting a discovery or spinning out a company is seldom problematic, but the real challenge is making science *fit* in the established socio-technical structures of producers and users (Ibid: 10). The necessity of reaching a fit between the new and the old suggests that several compromises will be necessary to continue the innovation journey, because of the many conflicts between the various actors involved, due to their diverging agendas and different resources (Latour, 1986). In fact, innovation in general, and the commercialization of science in particular, is not a matter of simple "adoption" by passive users, but of painful and costly "adaptations" between the new solution and the surrounding context (Akrich, Latour & Callon, 2002: 209; Van de Ven et al., 1999).

Commercializing science requires therefore embedding science in complex networks in order to be able to extract economic values from it, which can be possible only if the existing physical and immaterial resources structure can be *interfaced* favourably with that scientific discovery (Håkansson & Waluszewski, 2002). We define the "embedding process" of science as the emergence of *interfaces* between a focal scientific discovery and the other material and immaterial resources necessary for *developing*, *producing* and *utilizing* it, so to turn that science into an innovation (Baraldi, Gregori & Perna, 2011: 839; Baraldi & Strömsten, 2006: 58; Håkansson & Waluszewski, 2002: 225-8).

The "resource interaction perspective" (Baraldi, Gressetvold & Harrison, 2012) provides a useful toolbox for investigating the resources embedding science: this perspective not only classifies these resources into physical (products and facilities) and social (organizations and relationships) according to the 4Rs model (Baraldi & Bocconcelli, 2001; Håkansson & Waluszewski, 2002), but it also penetrates into how the (re)combinations among these resources create their values. In particular, the concept of "resource interface" indicates the specific contact points and connections between two resources, showing how they fit into each other and affect each other's technical or social features (Baraldi, 2003: 17-23; Håkansson & Waluszewski, 2002: 214-5). Dubois and Araujo (2006) distinguish between *technical* resource interfaces, when they connect two physical resources (e.g., two products), and *organizational* interfaces, when they connect two social resources (e.g., a relationship and an organization). Moreover, the "mixed" interfaces, between for instance a facility and a relationship, can also be pivotal during an embedding process (Baraldi & Strömsten, 2006).

The 4Rs model and the concept of resource interface can be applied to understanding the embedding of science by starting from a focal discovery, which can be viewed as a *product* being developed, whose main features are initially knowledge-related, but which need to become progressively more materialized and physical. By analyzing the technical, organizational and mixed interfaces between the focal resource science and the surrounding ones (other scientific discoveries, existing products, facilities, organizations and relationships), it becomes possible to see clearly how science gets transformed by being combined (interfaced) with these resources. This analysis needs to be extended to all resources stretching from science to end-users in a commercial setting or in the wider society.

In fact, in order to become embedded as an innovation, science needs to be interfaced with resources found in *all* these three settings: a *developing*, a *producing* and a *using* one (Håkansson & Waluszewski, 2007; Ingemansson & Waluszewski, 2009; Baraldi, Gregori & Perna, 2011). The *developing* setting includes actors, such as universities and R&D labs, who create new solutions by combining resources in new ways, and typically rewards cutting-edge knowledge and unique solutions (Håkansson & Waluszewski, 2007; Ingemansson & Waluszewski, 2009: 23); the *producing* setting includes actors, such as manufacturing firms and distributors, who industrialize the production and shipment of products in such a way to attain high efficiency and exploit their large-scale investments (Ibid: 24); the *using* setting, finally, includes direct and indirect users, in the form of either organizations or private persons, who are mainly concerned with solving specific problems in their daily operations or lives in convenient and simple ways (both economically and emotionally).

The three settings can overlap in terms of actors and when they become relevant for an innovation, with the using setting being present also from start, for instance when it comes to user-driven innovation (von Hippel, 2007). However, the three settings do follow diverging logics and their resources will put conflicting pressures on the original piece of science. Especially the production and using setting will require strong changes and adaptations in the science being commercialized, so to make it more “productified”, reproducible and reliable. But even if the resulting product will be superior than the incumbents from a mere scientific and technical point of view, the using setting can still create barriers to the new because of purchasing and using routines which are hard to break especially in the healthcare field (Wagrell and Waluszewski, 2009). Still, in order to become embedded, science needs to achieve interfaces connecting it to all the three settings, either via resources “located” in each of the three settings or via resources and actors that connect themselves the three settings (Baraldi, Gregori & Perna, 2011). Lacking such interfaces, that science will remain embedded in only one or two of the three settings, without becoming an innovation.

RESEARCH METHOD

Our method relies on an in-depth case study over the embedding process of the PET technology originating from Uppsala University. We conducted over 40 personal interviews with the involved actors belonging to the three settings of developing, producing and using, such as academic researchers, university managers, hospital doctors and managers, as well as company representatives. These first-hand sources were complemented with archival materials. This paper focuses on one of the key resources involved in the commercialization of PET technology, namely the *radiotracers*, the other two main resources being the *PET equipment* and *the knowledge/organization behind the PET center*.

In order to create the storyline specific for radiotracers, we first identified salient moments that were grouped into main periods characterized for instance by a particular actor controlling the PET technology; and then we re-organized the large empirical material in order to create a storyline centered on our focal resource – the radiotracer – but highlighting its *interfaces* with surrounding resources. We also applied the *three settings* framework – "developing", "producing" and "using" – as a tool to identify how interfaces emerged between the resources spread across the network embedding the PET technology. This approach helped us understand the effects commercialization has had on the network surrounding the technology. To accomplish this goal a substantial number of interviews have been carried out (see Appendix A), and archive material also been used to both supplement and corroborate the information obtained from the interviews.

This study is part of a broader research project concerning the commercialization of academic research, with a focus on science originated from Uppsala University. Therefore, we started our investigation from Uppsala University's innovation office (UU Innovation). Six interviews at the office helped us identify a project with some unique features, the commercialization and de-commercialization of Uppsala PET center. We eventually selected the PET center for an in-depth case study for a number of theoretical reasons related to our research purpose. First, the process had been going on long enough for there to actually be a product out on the market, as well as users of the product in question, which would enable us to investigate not only science-technology the developing setting, but also in the producing and using settings. Second, the PET center's interactions with industry encompassed a variety of commercial undertakings. Third, the PET center case deals with a network where three different spheres meet: academia, business and healthcare. Finally, the PET center made a quite unusual circular journey over the course of eight years, that is, commercialization followed by de-commercialization.

We have made use of "snowball" sampling for the interviews, starting off, as mentioned above, at the Innovation Office, whose director provided names of people who had been involved in the PET process. Subsequently each of the respondents has been asked to name other relevant individuals. We have then tried to identify who the key individuals are, based on how often they are mentioned by respondents, and by tips from the people most deeply involved in the activities at and around the PET center. Representing such different spheres as university management, academic science, clinical research, healthcare, business development, business management and municipal politics, a total of 33 individuals have been interviewed for the PET center case study, adding up to total of 39 interviews for this study. The archive of the Uppsala County Council has also been very valuable, containing all minutes from meetings between Uppsala University and Uppsala County Council, as well as every public document relevant for the Uppsala County Council written about the PET center. Data was collected between 2009 and 2013.

THE CASE OF UPPSALA PET CENTER

Background

On April 29, 2002, Uppsala University signed a contract that would take the institution into unexplored territory, impelling an interaction between industry and academia thus far untried at Uppsala. After a full year of negotiations a large British biotech company, Amersham, had purchased a world-leading medical research center, the Uppsala PET center, which up until that point had been a part of the university. The acquisition had been welcomed by most of the university management as well as the leading scientists at the PET center, who saw the handing over of the ownership as the best way to ensure that the needs of the center, in terms of equipment, personnel and research facilities, would be catered to. A field of science requiring heavy regular investments in infrastructure, PET research had for years been putting a serious strain on the university research budget, and the Uppsala PET researchers were therefore grasping for an alternative source of financial resources. Commercializing the PET center was by all parties involved seen as a solution to the economic problems.

The new owners, Amersham, on their part naturally had expectations too, expectations of a nature befitting to a profit-seeking business; through the investment they hoped to quickly build up a competence within PET in their organization, to benefit from the unique know-how of the researchers in their R&D work, to create a strong relationship with the pharmaceutical industry, and to boost the valuation of the company and its stocks. Together with two other renowned PET centers, one in England (Hammersmith, London) and one in Finland (Turku) Uppsala PET center was tucked into a new venture called IMANET. But only two years after the acquisition Amersham itself was purchased by GE Healthcare, a part of the giant American corporation, meaning that Uppsala PET center once again found itself in a completely new ownership situation. Consistently making red numbers from the day it was taken over by Amersham, the PET center continued to lose money under GE as well.

No longer willing to sustain Uppsala IMANET, which was increasingly considered an economic drain, GE in 2008 proposed to Uppsala University and the university hospital – the single largest user of the services offered by the PET center and completely dependent on having close access to PET technology – that they take the center back for a symbolic sum. Thus, in 2010, after two years of negotiations, the PET center was de-commercialized and returned to public ownership. In the empirical account that follows this commercialization/de-commercialization journey will be recounted again focusing on the most basic (and tiniest!) constituent of the PET technology: the *tracer molecule*.

PET – the technology

Positron emission tomography, abbreviated PET, is a nuclear medicine imaging technique that has been in use since the late 1960s. PET is used as a tool both in medical practice, in research as well as in the pharmaceutical industry, and produces a three-dimensional picture of biochemical processes in the body. PET is used extensively in oncology to detect cancer tumors, to differentiate benign and malignant lesions, and to monitor response to treatment (Wagner, 1999). It is also used in neurology to better understand, diagnose and treat brain pathologies (e.g. Alzheimer and Parkinson) and psychiatry, where PET is widely used to study depression, schizophrenia and substance abuse. Another major field is pharmacology, where PET technique is employed to study both how a pharmaceutical drug is distributed in the body (biodistribution), and to what extent it blocks a certain protein.

In order to generate a PET image the patient needs to be injected with a substance that is labeled with radioactive material, so called radioisotopes, which are produced in a *cyclotron*, a type of particle accelerator. The substance on which the radioactive tag is placed can be a natural chemical that is normally used by our bodies such as glucose, or molecules resembling pharmaceuticals designed to bind to specific receptors in our cells. These tagged compounds are known as radiotracers. When the tracer is injected into the body, a positron will be emitted from the radioisotope as the radioactive matter starts to decay. The positron will travel a short distance, just a few millimeters, through surrounding tissue and then collide with an electron, thereby emitting energy that will be detected by a camera, the so-called *PET scanner*, as points of light. In other words, the radiotracers function as light beacons.

But how does the tracer know where in the body to go? As the tracer enters the body it functions more or less as a robot searching for its target and will accumulate in the part of the body they are modeled to go to. For instance, if one wants to find out where in the body cancer tumors are located, a tracer called FDG is often used which is an analogue of glucose, tagged with the radioisotope Fluorine-18. As malignant tissue consume more glucose than healthy tissue, FDG will build up in large concentrations around tumors, where they will be visible as illuminated spots in the PET scan. In the case of a pharmaceutical drug's distribution or occupancy study, the radioisotope is incorporated into a drug molecule (but without therapeutic effect) so that it will travel to the same cellular target as the drug. The tracer will then accumulate in the relevant part of the body and show exactly where in the body the drug travels or to what an extent a certain cellular target is blocked.

The steps to generate a PET image are the following: When the radioisotope has been produced in the cyclotron it is transported via pipes to a shielded nuclear radiation containment chamber, also known as *hot cell*. Inside the hot cell the radioisotope is combined with another substance, for instance glucose or a drug, as exemplified above. This step, where chemical methods are applied to integrate the radioisotope into a bigger and more complex molecule, is nowadays largely automated. The outcome of this synthesizing process is the tracer, which is then injected into the body ready for being scanned with a PET camera.

Tracers at Uppsala PET center

Founded in 1989, Uppsala PET center is the brainchild of the Uppsala scientist Bengt Långström, who back in the 1970s had gained world fame in his field for his ground-breaking work in PET chemistry. His most significant contribution involved invention of methods that made it possible to radically cut times for synthesizing tracers in the hot cells from weeks to only 40 minutes, including steps whose time was reduced from 48 hours to just 5 minutes. Långström's new methods gave impetus to a real surge of scientific work in PET, including especially a shift in research from *chemistry methodology* (whose difficulties had been considerably reduced by his discoveries) to *biological* problems and the development of new tracers. The Uppsala PET center consequently started to focus their research on creating new biologically relevant tracer molecules.

Developing tracer molecules resembles the development process for pharmaceuticals, relying on a funnel principle whereby a broad set of candidates is successively narrowed down to one substance to be taken through the necessary trials. But where the pharmaceutical industry has the resources to screen tens of thousands of substances and pick out the ones that work, the numbers of candidates PET researchers begin with are decidedly more modest, usually between 10 and 15. It may therefore go without saying that the pharmaceutical library of the drug industry is an important source of interesting molecules for developing PET tracers. PET researchers can obtain these molecules either for free through collaboration with a pharmaceutical company or by purchasing them. When IP rights are not at stake, information on interesting pharmaceutical molecules can also be found in scientific publications. In addition, there also exists a large pool of well-known substances where PET researchers can begin their search for promising molecular structures. In sum, PET researchers generally do not invent the chemical templates of tracers themselves but depend on external sources.

The three activities of Uppsala PET center
A key aspect of the PET center was that at its founding Uppsala University decided that it operations would be divided into three equally important parts, also from a financing viewpoint: *independent academic research*, *contract research* for the pharmaceutical industry and *clinical PET scans* for the university hospital. The radiotracer is the least common denominator in all three activities: it is the subject of independent research, the technology necessary to carry out fee-for-service studies with industry, and the technology that the university research hospital is dependent upon to do a PET scan. The three-legged division has been the platform throughout the development of the center although the ratios of the parts have varied over time, to a large degree depending on who the owner of the center has been. The remaining part of the empirical story is structured around this operational division and laid out for each ownership phase the PET center has been through: (1) the years as a university-owned unit, (2) the period as a commercial organization, and (3) the current state as a center co-owned by the university and the university hospital.

The university years

Independent science – the 5-HTP example:
The specialty of the Uppsala researchers has always been tracers marked with short-lived radioisotopes. One of the most important tracers developed by the center was 5-HTP, a compound labeled with carbon-11 (half-life of 20 minutes). This tracer was the fruit of a research collaboration between Långström and oncological endocrinology researchers at the university hospital that began in the mid 1980s. The two research teams developed target-seeking substances specifically for endocrine tumors, and 5-HTP was one of the very first of this set of tracers. The PET center was originally developing these tracers not for clinical reasons, but purely for scientific purposes and it was in discussions with clinicians that they realized that some of them could be of clinical use as well.

In the early years of the collaboration, before the physical PET center was established, Långström would produce small quantities of the substance and put it in a little box. He would then get in a car together with the patients, the professor of oncological endocrinology, Kjell Öberg, and a PhD student, and drive to a factory nearby that produced PET cameras, where the scans would be performed. As time went by the PET center was established and now that the PET researchers had a scanner of their own the trips out to the scanner factory were no longer necessary. However, it became clear that the use of 5-HTP was unlikely to spread to other PET facilities: while these radiotracers were highly useful for finding the exact position of small tumors, they were extremely tricky to produce (21 enzymatic steps required highly skilled chemists) and carbon-11's short half-life required a costly and difficult to service cyclotron in absolute proximity of any using hospital. Nevertheless, given the excellent results in localizing small endocrine tumors, several research groups over the years have come from abroad to learn how to synthesize 5-HTP at Uppsala PET center.

To this day however, the only PET research group outside Uppsala that has learned to master the 5-HTP process is a PET center in Groningen, Netherlands. Interestingly, the Groningen center is the only place that possesses the exact same synthesis apparatus as Uppsala, a piece of machinery that Långström built himself for both centers. As a consequence, patients showing signs of hormone producing tumors and needing to have the tumors localized, merely have two places in the world to turn to. Being the pioneers and foremost specialists in the method, the university hospital in Uppsala has attracted a great number of paying patients over the years from all over the world, about 250 yearly.

PET services for the university hospital:
Uppsala university hospital has always been completely dependent on the PET center, using the technology to diagnose disease, as well as to oversee response to therapies. When the PET center was formed the agreement was that the hospital would purchase a fixed number of PET scans every year, thus financing part of the PET center's operations. The bulk of the PET scans performed have been made with the FDG tracer to identify cancer tumors. Since PET is an expensive technology, and since there may exist cheaper alternatives, the actual number of PET procedures that have become part of clinical routine is limited. But if the goal is to really *understand* a medical condition and the biological mechanisms, PET constitutes a very valuable tool. Also, some radiotracers that have not yet become clinical routine may eventually become more than just the subject of basic research and start approaching the clinic, as the example of 5-HTP shows. After years of extensive research, the use of the tracer 5-HTP for the detection of neuroendocrine tumors, as well as the monitoring of therapies for endocrine cancer, is now standard routine in the medical practice at the university hospital.

Contract research:
The PET scientists' collaboration with the drug industry played an important role for the center's finances from the very beginning. Although slow at first, the fee-for-service business really started to gain momentum towards the late 1990s, with the center conducting experiments for more or less all major pharmaceutical players. To be able to run the tests specified by the drug companies the PET researchers would produce the tracer molecules, mostly FDG, in their facility. FDG completely dominates contract research and clinical utilization, while most other tracers are mainly considered as basic research tools. One of the reasons for this domination of FDG can be attributed to the fact that the fluorine-18 isotope, which is the radioactive label of FDG, has a half-life of about 110 minutes, much longer than the 20 minutes of carbon-11. The principal advantage of a compound with a long half-life, such as FDG, is obvious: the radiotracer can be manufactured in bulk and transported to the sites where it is to be used. Hence the industrial preference for molecules labeled with fluorine-18 and, as a result, the prevalence of FDG in the contract research studies the Uppsala PET center signed up for. It was partly the center's success in contract business that kindled ideas of expanding the center. And such an expansion called for heavy investments, which is why Uppsala University and the PET center eventually turned to industry.

In the commercial sphere

Amersham's strategy:
Amersham stepped into its new role as the owner of the Uppsala PET center intent on learning about PET science as well as increasing its own stock market capitalization. But Amersham's most important strategic goal was getting access to the molecular libraries of drug companies. These libraries contained "failed" molecules: molecules that had not worked out as pharmaceuticals. A pharmaceutical molecule is normally supposed to go to its target in the body and stay there for a long time while it treats the ailment. Instead of lingering around a target, however, a failed molecule is one that dissipates too soon, or in other ways falls short in achieving its anticipated therapeutic effect. But exactly the properties that make a molecule inadequate as a drug make it an ideal candidate for a PET tracer molecule: acting as an imaging agent with as little effect as possible on the body. Therefore Amersham wished to get access to these failed molecules in their hunt for new future tracer molecules.

Believing that pharmas had several such unsuccessful compounds, while also recognizing the growing importance of PET technology for drug development, Amersham felt that a close collaboration with the pharmaceutical industry would be rewarding for both parties. To make all this happen Amersham wanted to use its newly acquired PET centers, including Uppsala. The idea was that the PET centers, all of whom had extensive networks including all major drug companies, would do contract research for them, thereby building good relationships between Amersham and big pharmas. These relationships – so the thinking went – would eventually induce the drug companies handing over their molecular libraries to Amersham. However, this part of the strategy, which was simply taken over by GE Healthcare after the acquisition of Amersham, never worked out since the pharmaceutical companies in no way wanted to relinquish control over their IP. The portion of the strategy that steered Uppsala PET center toward an increased focus on contract research remained however.

Research: independence vs. fee-for-service

The acquisition of Amersham by GE Healthcare brought a focus on profit, increasing revenues and cutting costs in the operations at the Uppsala PET. This put independent research in a precarious situation. As the resources needed to conduct experiments were being cut so as to alleviate the financial problems of the company, independent research began to decrease to such a degree that it risked being almost entirely squeezed out. Apart from dampening the spirits of the PET researchers, this dwindling of free research had an adverse effect also on contract research. The PET center had always had a distinct scientific profile, never doing contract research solely to make money, and accepting only industrial assignments they were certain of carrying out with great precision. But although service quality is vital to obtaining new contract research assignments, it is not the only factor pharmaceutical companies consider when they look for academic collaboration partners. In order to stay attractive on the fee-for-service market a PET center has to maintain a certain academic quality, which is only possible if a considerable part of the center’s operations is devoted to free research. As the priority at Uppsala now was contract research, and since the opportunities to pursue independent research projects were seriously constrained, the center started to lose status and attractiveness on the contract research market. In spite of this, the GE's strategy did not change, meaning that tracers were to be produced primarily for PET experiments for industry, and clinical applications for the university hospital.

Another important part of the owner’s strategy was that Uppsala PET center contribute commercially interesting ideas, which the Uppsala researchers and the Amersham/GE researchers would then pursue and develop together. But the Uppsala PET center’s innovative spirit or scientific skill did not help them come up with research ideas that appealed to their owner. The Uppsala team consisted of academic scientists who had never been employed by a company before, and the research problems that interested them for the most part tended to be lacking in commercial potential. The researchers from Amersham/GE on the other hand were trained to identify research questions of business relevance, but at the same time they did not possess the same cutting-edge knowledge in PET as did the scientists at Uppsala. As a consequence the collaboration between the two research groups never took off. Instead the Uppsala researchers devoted most of their time to contract research.

Tracers at the hospital:

The acquisition by Amersham entailed an agreement that services to the hospital were to be delivered as before. But while the needs of the hospital had not changed, Amersham changed the price list: the tracers, which hitherto had been sold as a package deal together with the PET scan at a price lower than the actual production cost, would no longer be sold at a loss.

Instead the hospital would be charged the cost price of the production of the tracer and the PET scan. The hospital reacted strongly against Amersham's/GE's approach to pricing, arguing they simply had no way of paying that kind of money. After some discussion, Amersham agreed to reduce its suggested price for FDG, while increasing to a full cost coverage that for 5-HTP. Consequently, PET scans for patients with endocrine cancer became much more costly to perform.

Back in public ownership

All stakeholders –GE Healthcare, the university, the PET researchers, and of course the management and doctors at the hospital – had their own ideas as to what the use, development and production of tracers would look like after the university hospital and the university assumed ownership of the PET center in November 2010. The doctors expected quicker handling of PET scans for patients, the university hoped to see a revival in academic research, including development of new tracers, while the PET researchers wished for good conditions to do research. And importantly, GE Healthcare, now freed from any responsibility for infrastructure and personnel, still wanted to assign work to the researchers at the center. The new contractual arrangement involved, amongst other things, a so-called guarantee sum to be paid out by GE to the hospital for three consecutive years in exchange for having the PET center at their disposal. What GE wanted was to have the Uppsala researchers conduct experiments for the company’s own R&D, as well as doing contract research for the drug industry, but with GE as the contractor. The price for all these studies would be covered by the guarantee sum paid to the hospital.

Contract research affecting production and clinical use of tracers

During the first year of the new regime the arrangement described above had clear consequences on tracers. By covering a good portion of the annual running costs of the PET center via the guarantee sum, GE had significant influence over the scheduling of what type of isotopes to produce in the cyclotron and which tracers to synthesize in the hot cells. In short, the production of tracers needed to match GE’s needs. As the research studies conducted under GE’s oversight are geared towards industry, the isotope chiefly being used is fluorine-18, due to its relatively long half-life. The fact that GE to a considerable degree was able to control the schedule of tracer production put the university hospital in a situation where they were not in complete command of the research center that they owned. The effect of this was palpable for the units of the hospital in need of tracers that are not fluorine-based, notably the department of endocrine oncology, which requires the carbon-11 labeled 5-HTP for its patients. Since the cyclotron was often busy making fluorine-18 radioisotopes for GE’s internal projects and their fee-for-service projects, it would sometimes be weeks before the endocrine oncology unit could have radiotracers produced. However, during 2012 this situation, which had posed a serious problem for the department of endocrine oncology for so long, was resolved, meaning that the clinic is now finally enjoying the benefits of actually being in control of the PET facility.

Independent research:

With the hospital is charge of the clinical part, the university manages the *pre-clinical* part of the center, with scientists now allowed to pursue independent research projects again, which is visible in the past year’s steep increase in publications related to PET. Nonetheless, the research group, which used to include around 30-40 researchers during its hey-day, today consists of merely a handful of researchers, is subsisting on a tight budget, and still has not found a professor to lead the work (Långström retired in 2010). The world-leading position is long gone, lost during the years when free research was put on hold. Still, the team is looking ahead, hopeful to soon be successful in tracer development again.

ANALYSIS

Our analysis of the PET center story examines the winding path of the commercialization and de-commercialization processes with the radiotracer as the focal point. We will also investigate the resource interfaces involving radiotracers in the using, developing and producing settings. As shown in the empirical account, radiotracers have varying physical properties and are used for a variety of purposes. Some tracers have a long half-life, are easy to produce and can be shipped, while others are extremely difficult to synthesize and will decay so quickly that they must be used immediately on site. The properties of the tracers decide both their use and their value for the different actors involved. And it is exactly this question – which tracers are valuable to *develop* and *produce* and for what end they should be *used* primarily – that has been the locus of conflicts between the three main stakeholders, the mother company Amersham/GE Healthcare, the PET researchers, and the university hospital.

The clash of expectations, valuations and wishes tied to the PET center is the consequence of the triple-focus of the center: during its years as Uppsala IMANET the center was at once a commercial unit, an organization servicing the university hospital, and a place for independent research. The free science-spirited PET researchers divided up their time and efforts between three worlds: *curiosity-driven science*; *healthcare*; and *contract research*. In other words, even during the years of commercial ownership, many of the resources of the PET center were never exclusively devoted to making tracers to meet commercial objectives. Rather, to varying degrees resources have also been engaged in the use, production and development of tracers geared towards academic research and patient care.

We thus have an organization with a three-fold function, and hence the use, development and production of radiotracers are aligned with each of these functions: Tracers are used as a *scientific* tool in both pre-clinical and clinical research to learn more about biological processes in the body; they are used as a tool to develop new tracers; they are used as a *diagnostic* tool in patient care, as well as a tool to monitor patients' response to therapeutics; they are used as a *commercial* tool in pharmaceutical development in which PET researchers take part contracted by the pharmaceutical industry on a fee-for-service basis. And the tracers needed for this collection of activities all come out from the same facility: the Uppsala PET center. One important analytical ramification of this circumstance is that the developing, producing and using settings of the tracer strongly overlap both spatially and temporally, more than they do for other new technologies (see e.g., Baraldi, Gregori & Perna, 2011). This intermingling of the settings in both time and space will now be explicated in greater detail as we proceed to map out some vital resource interfaces in the three settings. We start from *technical/physical* interfaces and move then to *organizational* ones (Dubois & Araujo 2006).

Physical resource interfaces in overlapping settings

The perhaps most obvious interface shared by all three settings is that between the tracer and the facilities needed to manufacture it. The same apparatus is activated both for developing the tracer, producing it and using it. Put differently, it does not matter whether the tracers are destined to be used in an independent research experiment, a fee-for-service study, a routine PET scan of patients – radioactive isotopes must still be produced in a cyclotron and synthesized in the hot cells. In all three situations the tracers must subsequently be injected into a living subject that is then scanned by a PET camera, regardless of what the scan results will be used for. Further, when sorting through the resource interfaces of the tracer in the three different settings, one must first realize that several crucial interfaces between the equipment and other resources – such as chemical compounds, knowledge and living subjects – are common to all three settings, that is, occur in the developing setting as well as the producing and using contexts. This is the case since the PET center, as pointed out above, is the place where both development and production, and some of the use of tracers take place.

Now, as already touched upon, the settings – and therefore some of the resource interfaces – are not only partly *spatially* overlapping, but also *temporally* so. For instance, an experiment carried out as a step in the *development* of a new tracer inevitably involves the *production* of tracers, and may also, if the tracer under exploration is simultaneously tested clinically (both in patient care and clinical research, since these two activities often blur), also involve *using* setting. From this follows that many of the interfaces between the resources involved in these temporally and spatially coinciding settings, will be the same. One example where such an overlap occurs is the radiotracer 5-HTP. While PET scientists were doing all the chemistry lab work for the experiments, clinicians, in their capacity as both researchers and physicians, were taking part in the *development* efforts by involving their own patients in the testing. But the testing was not only testing since the tracer under development also helped in a very real way to diagnose the patients, the tracer was simultaneously being *used* clinically. And, implicitly, for this use and development to even happen, *production* of tracers was taking place. We now have a close look at a few of the interfaces in these overlapping settings.

1- Hot cells and researchers’ PET chemistry expertise in the producing and developing settings: The interface “cyclotron-hot cells”, as well as the interface “PET researchers’ chemistry expertise-hot cells” are crucial in, and therefore common to, both the producing and the developing settings. The latter of the two interfaces is especially noteworthy in the case of 5-HTP: both the skill and the apparatus required to complete the very complex synthesis of this particular tracer are so specific that only two centers in the world are able to do it, Uppsala and Groningen. Simply possessing the knowledge about the 21 enzymatic steps is not enough; it needs to be combined with a type of instrument in the hot cell which at this point only exists in Uppsala and Groningen. Essentially built by hand by a senior scientist, Långström, this particular piece of synthesis equipment is difficult to replicate. And failed attempts by researchers at centers elsewhere in the world indeed seem to indicate that there cannot be even the slightest deviations from Långström's hand-made machine if the synthesis is to work. In other words, a PET researcher’s theoretical knowledge of how to synthesize 5-HTP works only in combination with a unique piece of equipment. This signals therefore a very *deep* interface between these two resources, the knowledge and the machine, and it is so in the producing as well as the developing setting. This is naturally true for all types of tracers, but is especially well illustrated by the case of 5-HTP due to the specificity and singularity of both knowledge and apparatus involved.

2- Cyclotron and the PET scanners in the developing and using settings: If we stay with the example of 5-HTP, we see that because of the very short half-life of the carbon-11 isotope there would be no development or use of the tracer without a cyclotron placed in close proximity to a PET scanner. In the development of 5-HTP (or any other tracer for that matter) the researchers naturally needed to conduct experiments on both animals and humans, and immediate scanning after injecting the tracers were consequently necessary. Evidently, the same conditions are required in order to use the tracer in clinical practice. This was one of the reasons why both a proper cyclotron and a full body scanner were needed on site, and why driving out to a scanner factory with a jar of tracers, a patient and some scientists all crammed in a car was not a tenable solution. A real interface had to be created between the cyclotron, via the hot cells, and the scanners. Put differently, the close connection of the cyclotron and the PET scanner was a resource interface of vital importance to the developing setting and the using setting alike, and during the period when 5-HTP was being developed this interface was often crucial in both settings at the same time.

3- PET scanners and humans in the developing and using settings: Another resource interface already mentioned is the one between the PET scanners and the humans to be scanned. During the period when 5-HTP was being developed this interface too was essential to both the developing setting and the using setting simultaneously. The testing subjects here assumed the role of two resources at the same time: for the PET chemists *developing* the tracers the test people were “guinea pigs” for refining their technology, whereas for the clinical researchers, who were also medical doctors and *used* the tracers for health care, the human subjects were not only tests subjects but also patients.

The three interfaces presented above contribute to creating both temporal and spatial overlap of two or more settings. Moving beyond the example of 5-HTP and looking more broadly at the development, production and use of tracers at Uppsala PET center we recognize a bundle of other interfaces that are *shared* between different settings in space, if not always in time. If not the entire interface is shared, then at least one of the resources in a resource interface is, making for a potential, or full-blown, conflict. Once again, a closer inspection of the use and production of tracers will illustrate such a situation.

Sharing physical resources: mixed interfaces

As pointed out in the beginning of this analysis the disagreement between Amersham/GE, the PET researchers and the university hospital can be viewed as a consequence of each organization’s goal concerning tracers – indicating a *mixed* interface (Baraldi & Strömsten, 2006). Whereas Amersham/GE primarily wanted tracers to be used for experiments within contract research, company-specific internal development projects and FDG-based clinical routine scans, the hospital wished to get any tracer they wanted produced for their doctors, for both patient care purposes and for clinical research projects. The PET researchers on their part wanted to use tracers mainly for research projects they were interested in, a goal that generally was possible to reconcile with the needs of the hospital as far as tracer production was concerned. But all in all, there was a conflict between the three stakeholders concerning what purposes various physical resources – cyclotron, scanners, hot cells, test subjects – should be employed for. Let us see two such concrete examples.

1- The fluorine-18 isotope, the carbon-11 isotope and users in the using setting: Due to its longer half-time Amersham/GE generally favored the production of the fluorine-18-based FDG, since this feature made FDG shippable, widely usable and hence commercially valuable. In other words, there is a potentially strong interface between fluorine-18 and many users, which explains Amersham's/GE's preference for this particular isotope. FDG can be sold to nearby hospitals for diagnostics and is especially used in the fee-for-service studies for the pharmaceutical industry. Furthermore, the university hospital as well has always needed FDG for their oncology practice, thus constituting yet another user for the fluorine-18 isotope produced in Uppsala.

But the hospital also needs the carbon-11 isotope to be produced for the synthesis of 5-HTP tracers for patient care. While the interface “carbon-11-users” is of very little economic value to Amersham/GE, it is very valuable to the hospital because carbon-11 is a component of the 5-HTP tracer which draws a lot of paying patients to the hospital. And needless to say, for the patients themselves carbon-11 has a value that may not be expressed in economic terms. Furthermore, academic researchers need for their research projects all types of different tracers – and therefore different isotopes, but these users do not contribute any economic value to Amersham/GE’s IMANET business. All in all, the a using setting consisting of multiple and very heterogeneous users, in terms of needs and willingness to pay, makes the two interfaces “fluorine-18-users” and “carbon-11-users” troublesome to handle at times. Basically, the short usable time of both tracers (i.e., they cannot be stored for future use) and the capacity constraints of the PET infrastructure allow only one of these interfaces to exist at the same time in the using setting: the involved organizations have to prioritize one interface against the other every time. The impossibility of producing simultaneously tracers for both user interfaces caused a lot of conflicts, with the hospital feeling that their needs always came second to those of Amersham/GE, as we can see in the next interface.

2- The company, the hospital and the cyclotron in the producing setting: There are two reasons why it is necessary to choose between producing fluorine-18 and carbon-11: firstly, both isotopes have a short half-life and therefore cannot be stored for later use (110 or 20 minutes do not really matter here) and, secondly, Uppsala PET center has only one cyclotron, which has to be shared between the projects run by Amersham/GE, the scientists’ independent research, and clinical users. From the time that the PET center was commercialized and well into the first year as a de-commercialized unit, the sharing of this resource was fraught with conflict. The problem here was that all the stakeholders needed one and the same resource, the cyclotron, to be activated in the producing setting. The fact that this setting contains interfaces that are mutually exclusive causes a cascade effect in the using setting, where, as discussed above, user interfaces involving tracers labeled with different isotopes cannot co-exist in the same time. The reason for this is that the PET equipment can only produce one tracer at a time, making it possible to utilize only that tracer right after.

Organizational interfaces

So far our analysis pointed how the same physical resources at the PET center have often been activated in two or more settings, often through deep interfaces with other physical resources, which contributed to *embedding* the scientific discovery of tracers in all three setting. However, deep interfaces also made *conflicts* arise due to the impossibility of substituting one resource for another – illustrated for instance by the tension around the cyclotron, a piece of equipment absolutely indispensable for the production of tracers. Nevertheless, as we go beyond *physical* and *mixed* interfaces to look at *organizational* ones the picture is quite different: the interfaces between many of the organizational resources relevant to the use, development and production of tracers are weak, or barely exist at all despite efforts to create them. Let us examine a pair of these interfaces to illustrate this point.

1- Amersham/GE’s strategy and the pharmaceutical industry in the producing and using settings: Amersham’s and GE Healthcare’s strategy for IMANET aimed specifically at establishing tight relationships with pharmaceutical companies by conducting fee-for-service studies. This fee-for-service interaction was the means to build up enough trust to obtain access to the drug industry’s molecular libraries. The much coveted resource in these libraries were IP rights for so-called failed molecules, which would help PET researchers developing new tracers. But despite Amersham and GE's efforts in building relationships with pharmaceutical companies, the drug industry showed little or no inclination to give up any of their IP. The interface between IMANET and the drug companies therefore never deepened in the crucial *developing* setting for new tracers, and existed only *weakly* in the producing and using settings, where fee-for-service studies meant that pre-determined tracers prescribed by the pharmaceutical firm had to be produced and used. Nevertheless, had the interface been deeper there would have been quite another picture, where the IP rights would have furnished new tracer development, placing the interface also in a developing setting. Additionally, organizational interfaces in the using and producing settings would have been richer, with larger volumes of tracers produced and used, including new ones developed at Uppsala.

2- Uppsala PET researchers' knowledge and Amersham/GE researchers' knowledge in the developing setting: The mother company expected to benefit from the PET center's major resource, namely its expertise in PET chemistry: Amersham wanted to set up collaborations between its own researchers and the Uppsala PET researchers. Two sets of knowledge – two sets of organizational resources – would thus be brought into contact. However, the interface between the two bodies of knowledge could not be created: on the one hand the Uppsala researchers possessed a deep understanding of PET chemistry which the Amersham/GE researchers lacked the capacity to fully absorb; on the other hand the researchers at the mother company were skilled at identifying commercially interesting research, which the academic researchers at Uppsala never really provided. Uniting the two capabilities was an excellent idea in theory, but proved much more difficult to do in practice; the two knowledge resources did not really fit each other and remained only weakly interfaced throughout most of the eight years the PET center was owned by Amersham/G E.

These two key organizational interfaces point to the frailty of Amersham/GE's interaction with both the PET center and the pharmaceutical industry, two organizations which were essential to IMANET's success as a commercial venture. Whereas the *physical* interfaces, as well as some of the *mixed* ones (e.g., knowledge and equipment) were deep, the *organizational* interfaces of Amersham/GE's strategy with the PET center's key organizational resource (PET chemistry knowledge) and with the pharmaceutical industry were weaker. But in spite of their looseness, organizational interfaces in general contributed to the density of physical resource interactions, enhancing the tension between the main stakeholders and intensifying the struggle for physical resources, as the predominance of business-geared activities pushed independent research and patient care into the margins.

CONCLUSIONS: RESEARCH FINDINGS AND CONTRIBUTION

Our analysis reveals that the complexity of commercialization processes derives from the fact that one and the same embedding process can combine different mechanisms for commercializing science, namely linear spin-out funnels (Clarysse et al., 2005) such as the transformation of the PET center into a company, and collaborative interactions (Jacobsson & Perez-Vico, 2010; Nilsson, Rickne & Bengtsson, 2010), such as those between the PET center and drug companies. Moreover, these different mechanisms can co-exist or appear at different moments in time, including even the extreme possibility of reversing the linear order of commercialization (i.e., from science to business) in favor of a "re-scientification" of commercial activities: in fact, the PET case entails first a spin-out and then a "spin-in" of science. These turns in the innovation process depend on how the resources across the three setting of developing, producing and using PET radiotracers were interfaced.

More precisely, commercialization was driven by costly technical interfaces (from radioactive isotopes to PET scanners), which were also well functioning and deep enough to sustain the very commercialization. The embedding of radiotracers succeeds across the three settings thanks to *technical* interfaces that exist in two or more setting and make them overlap. But embedding across *mixed* and especially *organizational* interfaces is weaker and eventually causes the de-commercialization of the PET center. Our case is therefore particularly interesting as it contradicts the typical situation in the commercialization of science: easier embedding across organizational interfaces, since actors are willing to agree on many issues provided that technical issues are solved, usually thanks to the relationships they build; more difficult embedding across physical/technical interfaces due to existing investments, competing technologies, capacity constraints etc.

The PET case shows instead that radiotracers became embedded at technical/physical level across all three settings of developing, producing and using, much thanks to the fact that they had to overlap due to the technical complexity (e.g., short half-times of isotopes) of the new solution. Instead embedding was not achieved at the level of organizational interfaces, due to lack especially of strong relationships with big pharma that could sustain economically the whole commercial venue. But the first problems became visible already in the mixed interfaces, such as conflicts in sharing resources within one and the same setting, including the using setting. Thus, the lack of embedding at organizational level simply slashed the economic sustainability of the whole resource combination “PET-company” and was at the origin of the de-commercialization of the PET center.

A major contribution of this paper is showing how commercializing science may include linear elements, epitomized by university spin-offs or patents/licenses on scientific discoveries, but the process is driven, in unexpected directions, by the *emergence* or *lack* of interfaces among the resources spread in the three settings of developing, producing and using, which all three need to be connected if a discovery has to become an economically viable innovation accepted and utilized by users (Håkansson & Waluszewski, 2007).

References

Akrich, M., Callon, M., & Latour, B., 2002, The Key to Success in Innovation PART II: The Art of Choosing Good Spokespersons, *International Journal of Innovation Management*, Vol. 6. No. 2, pp. 207-225.

Balconi, M., Brusoni, S., & Orsenigo, L., 2010, In defense of the linear model: An essay, *Research Policy*, Vol. 39, pp. 1-13.

Basalla, G., 1988, *The Evolution of Technology*, Cambridge University Press: New York.

Baraldi, E., 2003, *When information technology faces resource interaction. Using IT tools to handle products at IKEA and Edsbyn*, PhD Thesis, Department of Business Studies, Uppsala University.

Baraldi, E., & Bocconcelli, R., 2001, The quantitative journey in a qualitative landscape. Developing a data collection model and a quantitative methodology in business network studies, *Management Decision*, Vol. 39, No. 7, Sept. 2001, pp. 564-577.

Baraldi, E., & Strömsten, T., 2006, Embedding, producing and using low weight: Value creation and the role of the configuration of resource interfaces in the networks around Holmen's newsprint and IKEA's Lack table, *IMP Journal*, Vol. 1, Issue 1, pp. 52-97.

Baraldi. E., Gregori, G. L., & Perna, A., 2011, Network evolution and the embedding of complex technical solutions: The case of the Leaf House network, *Industrial Marketing Management*, Vol. 40, No. 6, pp. 838-852.

Baraldi. E., Gressetvold, E., & Harrison, D., 2012, Resource interaction in inter-organizational networks: Foundations, comparison, and a research agenda, *Journal of Business Research,* Vol. 65. No 2, pp. 266-276.

Bush, V., 1945. *Science: The Endless Frontier. A Report to the President.* United States Government Printing Office, July, Washington, DC.

Clarysse, B., Wright, M., Lockett, A., Van de Velde, E., & Vohora, A., 2005, Spinning out new ventures: a typology of incubation strategies from European research institutions, *Journal of Business Venturing*, Vol. 20, pp. 183-216.

Dasgupta, P. & David, P.A., 1994, Toward a new economics of science, *Research Policy,* 23, pp. 487-521.

Dubois, A., & Araujo, L., 2006, The Relationship between Technical and Organisational Interfaces in Product Development, *IMP Journal*, Vol. 1, Issue 1, pp. 21-38.

Grandin, K., Wormbs, N., & Widmalm, S. (eds.), 2004, *The Science-Industry Nexus. History, Policy, Implications*, Science History Publications: Sagamore Beach, MA.

Elzinga, A., 2004, The New Production of Reductionism in Models Relating to Research Policy, In: Grandin et al. (eds.), *The Science-Industry Nexus. History, Policy, Implications*, Science History Publications: Sagamore Beach, MA, pp. 277-304.

Etzkowitz, H., 2002, *MIT and the Rise of Entrepreneurial Science*, Milton Park: Routledge.

Etzkowitz, H., 2004, The evolution of the entrepreneurial university, *International Journal of Technology and Globalization*, Vol. 1, No. 1, pp. 64-77.

Håkansson, H., & Waluszewski, A., 2002, *Managing Technological Development. IKEA, the environment and technology*, Routledge: London.

Håkansson, H., & Waluszewski, A., (eds.) 2007, *Knowledge and Innovation in Business and Industry. The importance of using others*, London, New York: Routledge.

Ingemansson, M., & Waluszewski, A., 2009, Success in Science and Burden in Business. On the Difficult Relationship between Science as a Developing Setting and Business as a Producer-User Setting, *IMP Journal*, Vol. 3, Issue 2, pp. 20-56.

Jacobsson, S., & Perez Vico, E., 2010, Towards a systemic framework for capturing and explaining the effects of academic R&D, *Technology Analysis & Strategic Management*, Vol. 22, Issue 7, pp. 765-787.

Latour, B., 1987, *Science in Action*, Harvard University Press: Cambridge, MA.

Nilsson, A.S., Rickne A., & Bengtsson, L., 2010, Transfer of academic research: Uncovering the grey zone, *Journal of Technology Transfer*, Vol. 35, Issue 6, pp. 617-636.

Pavitt, K., 1984, Sectoral patterns of technical change: Towards a taxonomy and a theory, *Research Policy*, Vol. 13, pp. 343-373.

Pavitt, K., 2004, Changing Patterns of Usefulness of University Research. Opportunities and Dangers, In: Grandin et al. (eds.), *The Science-Industry Nexus. History, Policy, Implications*, Science History Publications: Sagamore Beach, MA., pp. 119-131.

Perkmann, M., & Walsh, K., 2007, University–industry relationships and open innovation: Towards a research agenda, *International Journal of Management Reviews*, Vol. 9, Issue 4, pp. 259-280.

Powell, W. W. & Owen-Smith, J., 1998, Universities and the Market for Intellectual Property in Life Sciences, *Journal of Policy Analysis and Management*, Vol. 17, Issue 2, pp. 253-277.

Rosenberg, N., 1994, *Exploring the Black Box- Technology, Economics, and History*, Cambridge University Press: Cambridge, UK.

Salter, A. J., & Martin, B. R., 2001, The economic benefits of publicly funded basic research: A critical review, *Research Policy*, Vol. 30, Issue 3, pp. 509-532.

Tidd, J., Bessant, J., & Pavitt K., 2001, *Managing innovation. Integrating technological, market and organizational change*, Second edition, Chichester: Wiley.

Van de Ven, A., Polley, D., Garud, R., & Venkataraman, S. 1999, *The innovation journey*, New York, Oxford: Oxford University Press.

von Hippel, E. (2007). Horizontal innovation networks – by and for users, *Industrial and Corporate Change*, Vol. 16, No. 2, pp. 293-315.

Wagner, H. N, Jr., 1998, A Brief History of Positron Emission Tomography (PET), *Seminars in Nuclear Medicine*, Vol. 28, No. 3, pp. 213-220.

Wagrell, S., & Waluszewski, A. 2009, The problem of using (medical) innovations. *IMP Journal*, Vol. 3, Issue 2, pp. 57-85.

Wright, M., Clarysse, B., Mustar, P., & Lockett, A., 2007, *Academic Entrepreneurship in Europe*, Cheltenham: Edward Elgar.

Zucker, L. G., Darby, M. R., Armstrong, J. S., 2002, Commercializing Knowledge: University Science, Knowledge Capture, and Firm Performance in Biotechnology, *Management Science*, Jan 2002, Vol. 48, Issue 1, pp. 138-153.

Appendix A: Sources of data

General UU Innovation/ UUAB interviews

Lars Jonsson, 2009-09-30, Uppsala

Mateo Santurio, 2009-10-05, Uppsala

Mateo Santurio, 2009-10-13, Uppsala

Lars Jonsson, Lars-Eric Larsson (*meeting*), 2009-10-13, Uppsala

Lars Jonsson, Lars-Eric Larsson, Karin Meyer-Rosberg (*meeting*), 2009-12-09, Uppsala

Gerard Pettersson, 2009-12-09, Uppsala

PET case interviews

Bengt Långström, 2010-02-05 and 2011-01-12, Uppsala

Lars Jonsson, 2010-03-30, Uppsala

Bo Sundkvist, 2010-11-17, Uppsala

Ulf Pettersson, 2010-12-09 (interview by telephone)

Gunnar Antoni, 2010-12-06 and 2011-01-28 Uppsala, 2011-03-25 (follow-up interview by telephone), 2013-03-19 (interview by telephone)

Andy Browning, 2010-11-30, Uppsala

Marianne Andersson, 2010-12-14, Uppsala

Erik Hemmingsson, 2011-09-02, Uppsala

Mats O. Karlsson, 2011-02-15, Uppsala

Kjell Öberg, 2011-02-17 and 2013-02-27, Uppsala

Anders Grundström, 2011-02-19, Uppsala

Britt Skogseid, 2011-02-22, Uppsala, and 2013-02-25 (interview by telephone)

Ulf Haglund, 2011-05-06, Uppsala

Martin H:son Holmdahl, 2011-05-07, Uppsala

Göran Beijer, 2011-05-17, Uppsala

Eva Telne, 2011-05-19, Uppsala

Peter Ehrenheim, 2011-08-24, Uppsala

John Jeans, 2011-11-10, London

Lennart Thurfjell, 2011-11-15, Uppsala

Colin Archer, 2011-12-05, London

Geoff Lee, 2011-12-06, London

Stephen Peake, 2011-12-07, London

Bill Clarke, 2012-06-08, Milwaukee

Robert Dannals, 2012-06-11, Baltimore

Jindy Luthra, 2012-10-18, London