Commercializing Academic Research Results. The PET Center Case

Keywords: commercialization, innovation, university, research, science

In the industrialized part of the world the efficient promotion of innovation has become a top priority for governments wishing to strengthen their industrial competitiveness and national economy. The conception of innovation as a prerequisite for prosperity is not new, but rather an idea that has been expressed in political debates for decades (Eklund, 2007). What has been changing over the past fifteen years, however, is the notion of where this desired good is likely to emerge. Increasingly debates on possible strategies to boost innovation reflect the view that innovations should be based on science. In other words, the prevalent idea is that scientific discoveries constitute the fertile ground on which innovation could, and should, grow.

Ultimately, in the focus on science as an integral part of innovation, the role of scientific research and universities is brought into play. As producers of scientific knowledge, universities are regarded as an important contributor to, and even a natural starting point for, innovation. Believing that universities harbor an innovating capacity which has so far not been used to its full potential, policymakers now urge universities to make serious efforts to facilitate the transformation of scientific knowledge produced within academia into innovations on the commercial market. Many universities have taken the policy directions to heart, and are determined to play an active part in creating economic value from academic research.

In light of this, the overarching question that guides me at this stage of my doctoral project is: what may be the effect on the surrounding network when a university decides to commercialize academic research results? To investigate this question I have begun a qualitative case study on the Uppsala PET center. The PET center is a medical research center, which since its start in 1991, has been of crucial importance to both the Uppsala University and the public research hospital in Uppsala. The PET center was part of Uppsala University until 2002, when it was sold to the British biotech company Amersham, which in turn was acquired by GE Healthcare two years later. During the years that preceded the commercialization a significant deficit had been accumulating due to the costly operations of the PET-center. Selling the center to a commercial player was therefore regarded by both the university management as well as the head researchers at the center as the best way to ensure that the needs of the center, in terms of equipment and research facilities, would be catered to. The financial gain the sale of the PET center generated was used to strengthen the new university holding company and its innovation center. While the innovation center thus was given new financial muscles, the commercialization journey of the PET center turned out to be troublesome. After a few unprofitable years, which also involved a loss in research edge, the center was sold by GE to the university hospital in Uppsala in the fall of 2010. It seems that commercialization meant one thing for the university and quite another for Amersham and GE, and the failure to marry the logics of science with that of business eventually resulted in the PET returning to public ownership.

Introduction

In political discourse and policy, both within Sweden and internationally, knowledge and innovation are held to be the primary driving forces of economic growth. In the industrialized part of the world the efficient promotion of innovation is therefore a top priority for governments wishing to strengthen their industrial competitiveness and national economy. This conception of innovation as a prerequisite for prosperity is not new, but rather an idea that has been expressed in political debates for decades (Eklund, 2007). What has been changing over the past fifteen years, however, is the notion of where this desired good is likely to emerge. Increasingly debates on possible strategies to boost innovation reflect the view that innovations should be based on science. In other words, the prevalent idea is that scientific discoveries constitute the fertile ground on which innovation could, and should, grow.

Ultimately, in the focus on science as an integral part of innovation, the role of scientific research and universities is brought into play. As producers of scientific knowledge, universities are regarded as an important contributor to, and even a natural starting point for, innovation. Believing that universities harbor an innovating capacity which has so far not been used to its full potential, policymakers now urge universities to make serious efforts to facilitate the transformation of scientific knowledge produced within academia into innovations on the commercial market. In response to these calls many universities in industrialized countries have established an institutional infrastructure devised to efficiently connect academic researchers with industry (Mowery & Sampat, 2005). This infrastructure comprises e.g. OTLs (offices of technology licensing) and incubation centers, as well as holding companies and units for legal advice, all set up to make the journey from the research laboratory to industry smoother. Put differently, the universities have taken the policy directions to heart, and are determined to play an active part in creating economic value out of academic research.

As brilliant and simple as the idea of basing innovation on excellent research appears, it is easier said than done; in empirical studies the transformation of scientific research into business has been recognized as a cumbersome venture (cf. Ingemansson, 2010; Håkansson & Waluszewski, 2007). Turning scientific discoveries into commercial products that will find their way to actual users have thus been shown to be a very difficult enterprise, and market failure seems to be far more common than market success. A question that arises is: what can universities, in their increasingly active role in the commercialization of academic research, bring to the process? Really, what may happen when a university as an institution becomes an actor in the commercialization process? And what will happen to the piece of science that is being marketed?

With questions of this kind in mind I came across a peculiar commercialization project at Uppsala University, Sweden. To the extent that a "typical" academic spin-off story exists, this is not what will be examined here. In other words, what will follow is not an account of researchers forming a company based on their scientific discoveries. Instead, it is a story in which a university, with the help of its recently founded holding company, commercialized one of its research centers by selling it to a major British life science company, Amersham. It was the hope of the university that the research center, which over the years had become too expensive for the university to run, would become an organization able to sustain itself on its unique innovations and world-renowned expertise. Two years after the acquisition, Amersham was itself acquired by General Electrics Healthcare, meaning that the research center was now owned by one of the

world's largest corporations. But only four years later GE entered into negotiations with the university hospital in Uppsala, which was highly dependent on the center for its clinical work. In the fall of 2010 the hospital purchased the research center, which thus came full circle and returned to public ownership.

When listening to the accounts of the people involved and when reading the documents produced in relation to this commercialization project, what is gradually beginning to take shape is a story about great expectations and colliding interests. This is the story that will be explored in my paper, with a particular focus on the issue of the marketability of science, and on the encounter between the logic of science and that of business.

Purpose

The overarching question that guides me at this stage of my doctoral project is: what may be the effect on the surrounding network when a university becomes involved in a commercialization project? I intend to investigate this question by using the technology at the research center as my focal point. The journey of the center will be explored by studying the three different ownership contexts the technology is embedded in at different points in time, starting from when the university runs the center, via private ownership and finally back to public ownership, when the center is essentially owned by the public university hospital. I will then analyze the commercialization process by looking at the interaction between resources in a producing, developing and using setting.

Theory

When we want to grasp the commercialization process of a science-based product or service we need to pay attention to both the factors that influence the behavior and decisions of the actors involved, as well as to how the technology in question affects, and is affected by, this process. In other words, both organizational aspects, as well as technological and economic ones, need to be investigated in order to understand why a commercialization endeavor evolves the way it does. If we carry out such an investigation we will eventually end up with a picture that sprawls in all directions and lacks clear boundaries; it will contain a multitude of information on subjects as diverse as laboratory equipment and personal conflicts, as well as annual accounts and contracts. The challenge we then face is how to make sense of this disorderly collection of information. How do I navigate through the apparent mess of my empirical findings without getting sidetracked? How do I structure what I observe and hear to a coherent account that helps me understand what I set out to investigate? The answer is: by using a suitable theoretical tool. The theoretical tool I choose will not only help me structure my findings, but it will also influence what I see and hear, how I interpret my observations, what questions I ask, and more fundamentally, what assumptions I make. Put differently, the theoretical framework will function as a raster to reality (or to what we perceive as reality, depending on our epistemological and ontological convictions and preferences). For my study I have found the IMP network approach and the 4R model to be helpful in dealing with the questions at hand.

The IMP network approach

Resting on an interactive perspective, where economic, social and technological features of a

company are believed to be the outcome of the interaction with other companies (Håkansson, Waluszewski, 2007), a central concept in the IMP network approach is that of relationships. Håkansson and Snehota (1995) have described a relationship as a "mutually oriented interaction between two reciprocally committed parties" which is developing over time (1995, p. 25). Binding together activities, actors and resources from different organizations, relationships usually emerge due to the interdependence of outcomes between two parties, an interdependence which can be either negative, and have a constraining effect, or positive, creating new opportunities. Value creation is seen as dependent on the manner in which resources are combined within organizations and over technological and organizational borders. In other words, drawing upon Penrose's notion of heterogeneity of resources (1959), the value of a resource depends on how it is combined with other resources and how these combinations are used.

The 4R model

In order to analyze such resource combinations a research tool known as the 4R model has been developed within the IMP framework. The 4R model focuses on the interplay between resources and is used to investigate how resources are developed and used (Håkanson and Waluszewski, 2002). In keeping with Penrose's idea that "[a] firm is basically a collection of resources" (p. 68, 1959), an organization is viewed as consisting of four different categories of resources, two of which are physical and two that are organizational. The physical resources are products and facilities and equipment, while the organizational resources are organizational units and organizational relationships. Organizational units bind together physical and human resources that exist within these units; a piece of technology in one organization (or part of an organization) may for instance be combined with skills and experience in another, and this joining of resources may result in e.g. a new machine, or an improved way of working. Importantly, the organizational relationships which make this type of resource interaction possible, are not seen merely as a means to benefit from resources, but also as resources in themselves (Håkanson and Waluszewski, 2002). The combining of resources means that interfaces between resources are developed, and these interfaces have knowledge about specific resource combinations built into them. Rather than being simple and standardized, this knowledge is often specific and particular, implying that the introduction of something new is usually a slow process (Håkanson and Waluszewski, 2007). For instance, an interface between a machine and human skill is made up of knowledge how to operate that particular machine, and not just any type of machine. Any attempt to change a resource interface will create tension in other related resource interfaces, that is, each force of action will be counteracted by a reacting force (ibid). I believe this model can be fruitfully applied in my study as the journey of the PET center is very much characterized by a quest for, and conflict over, resources.

Three settings: producing, developing, using

For an invention to become an innovation, it has to be widely used (Tidd & Bessant, 2009). This means that a potential innovation has to get through not only the developing stage, but also survive in a producing and using setting (Ingemansson, 2009). Research within IMP and science and technology studies have indicated that the greater the difference between these three settings, the harder it will be for the invention to become an innovation (ibid). In my study I will use the model of the three settings to help structure the analysis.

Method

To investigate my research questions I am carrying out a qualitative case study. Up until this point I have conducted a total of fifteen interviews with individuals from Uppsala University, UUAB, the PET center, the university hospital and Uppsala county council, and I plan to begin interviewing people from former Amersham and GE in a few months. I have made use of document archives, as well as websites and newspaper articles relating to my research area. My empirical work is guided by an attempt to pinpoint the resources connected to PET in order to understand the effects commercialization has had on the network surrounding the technology. In order to do this I am using the 4R model.

Empirical findings

The Uppsala PET-center is a medical research center which since its start in 1991 has been of crucial importance to both the university and the public university hospital in Uppsala. PET is short for positron emission tomography and is a nuclear medical imaging technique. Before exploring the twists and turns of the PET center odyssey, it is a good idea to get an understanding of what this technique is about. Therefore the next section will explain the scientific basics of PET as well as how the technique is used, and what equipment is needed. Subsequently the empirical findings on the commercialization of the Uppsala PET center will be presented.

PET technology - what is it?

Positron emission tomography as we know it today has been in use for medical purposes since the late 1960s and early 1970s, although over time there has of course been continuous development of the equipment and chemical substances involved. Needless to say, PET rests on previous scientific advances; the technique would not exist without the cyclotron invented by Ernest Lawrence and his co-workers in the 1930s, the discovery of artificial radioactivity by Curie and Joliot in 1934, or the development of scanners and tomographic imaging - just no list a few of the scientific discoveries that made PET possible.

PET is a nuclear medicine imaging technique which is used as a tool both in medical practice and in research. The PET method produces a three-dimensional picture of processes in the body, which makes it possible to see what is going on in our organs and surrounding tissue. The medical uses of PET are plentiful; it is used extensively in oncology to e.g. detect cancer tumors, to differentiate benign and malignant lesions, and to monitor response to treatment (Wagner, 1999; interview Gunnar Antoni, 2010). It is also used in neurology to better understand, diagnose and treat brain pathologies, e.g. Alzheimer's disease and Parkinson's disease, as well as in neuroendocrinology, which is the study of the interplay between the nervous system and the endocrine system. Cardiology is another important area of application, as is psychiatry, where PET is widely used to study e.g depression, schizophrenia and substance abuse. Another major field where PET is used is pharmacology, where PET technique can be employed to study both how a pharmaceutical drug is distributed in the body (biodistribution), and to what extent a drug blocks a certain protein (drug occupancy¹).

¹Basically, in a drug occupancy study it is investigated what doses of a pharmaceutical drug is needed to block a certain percentage of the protein the drug binds to, so as to achieve the right therapeutic effect.

In order to generate a PET image the patient needs to be injected with a substance which is labelled with radioactive material, so called radionuclides. The radionuclides 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, water or ammonia, or molecules resembling pharmaceuticals that are designed to bind to specific receptors in our cells. These tagged compounds are known as radiotracers, or simply tracers. When the tracer is injected in the body of a patient a positron will be emitted from the radionuclide as the radioactive matter starts to decay. The positron will travel a short distance through surrounding tissue until it has lost most of its energy, and then it will collide with an electron, whereby the mass of both particles will be converted into pure energy. The particles are said to have been *annihilated* and the result of the annihilation, i.e. the energy, is visible as two gamma rays, or photons, and will be detected by the PET scanner as points of light. In other words, the radionuclides 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 (short for fluorodeoxyglucose) is often used. These are basically sugar molecules tagged with the radionuclide Fluorine-18 (18F), and they will build up in large concentrations around tumors, as malignant tissue has a higher metabolism for glucose than healthy tissue. The FDG molecules become trapped in the cells as the try to metabolize the glucose. The presence of the FDG will then show as illuminated spots in the PET scan, as protons from the tracer and electrons in the body are annihilated and gamma rays are given off right where annihilation takes place – around the tumors that is.

In the case of a pharmaceutical study, when the distribution or occupancy of a pharmaceutical drug is under investigation, the radionuclide is incorporated into a pharmaceutical molecule. The tracer thus resembles a pharmaceutical (although it does not function as a drug) and will bind to the same receptor² as the regular pharmaceutical, i.e. they have the same target in the body. Consequently the tracer will accumulate in the relevant part of the body and give the researcher information on where in the body the drug travels, alternatively to what an extent a certain receptor is blocked, depending on what question is being explored (distribution or occupancy).

The PET technique, with its ability to trace substances in our body, to diagnose disease and evaluate treatments, is thus an extremely important tool both within research, clinical practice and the pharmaceutical industry.

I. The Uppsala PET center -The university years, 1989-2002. Owner: Uppsala University

In July 1989 the decision was taken by Uppsala university and Uppsala county council³ to form the Uppsala PET center. The decision rested on the expectation that the establishment of a PET

A receptor is a protein molecule embedded in a cell, to which different kinds of signaling molecules (e.g. neurotransmitters, a hormone, a pharmaceutical drug, or a toxin) may attach.

³ Uppsala county council (Uppsala läns landsting) is responsible for healthcare in Uppsala county.

center would provide favorable conditions for Uppsala university and Uppsala university hospital (Akademiska hospital) to maintain their positions internationally, and also allow for a development in new areas through the access to new PET research equipment. It was determined that the task of the center would be to further research and development in positron emission tomography, provide service to clinical practice and carry out contract research. Up until that point the researchers at the center had belonged to the department of organic chemistry and had conducted their experiments in the basement of the research facility Gustaf Werner Institute⁴. Tired of working in the basement and without direct access to the equipment they needed, the decision to establish a special center for their research was welcomed by the researchers; after almost twenty years of PET research at the university, the scientific area would eventually get its own facility.

PET research at Uppsala University – the beginning

It was in the early 1970s that a PhD student in chemistry at Uppsala, Bengt Långström, started experimenting with substances tagged with the radioactive isotope carbon-11. Back in the 1960s and early 1970s there existed only a few very rudimentary substances labelled with radioactive material; researchers worked mostly with sugar molecules which were used to study cancer tumors, but there was not much else. The introduction of modern PET scanners in the 1970s however, resulted in an increased interest in working with the chemistry in PET, i.e. the synthesis of radio tracers. In other words, the question how to build chemical compounds that could be used as tracers started to receive much attention. It was around this time, in 1972, that Långström published an article on how to make a very simple organic molecule⁵. The molecule could be used to label plenty of different substances, and this finding was a scientific breakthrough which opened up for important new research in chemistry. All of a sudden the researchers had a new tool, a whole new way of making tracers, and this discovery spurred a veritable flood of research on the synthesis of tracers.

Långström's innovative contribution consisted primarily in his use of methods on how to make radio tracers. In chemistry there is a huge library of methods on how to produce different types of compounds, and as a chemist he was familiar with many of these. He started to try to apply these methods normally used in chemistry to PET, with the intention of finding out whether a chemical process that would usually take days, weeks or even months, could be done in a much shorter time. Since speedy handling is of the essence when dealing with short-lived radionuclides, methods that require days or weeks to complete the synthesis of a tracer are of no use. Långström's major achievement was thus that he actually succeeded in using chemistry methodology to produce radio tracers in much less time than had previously been done. Instead of spending months in a chemistry laboratory making a substance, the most common tracers could now be synthesized in 40-120 minutes in the hot cells⁶ in the PET laboratory.

In the early stages of PET research, where Långström soon became a leading figure, most efforts were concentrated on developing and refining these tracer production methods. Today PET researchers tend to think of methodology as the basics and the ordinary routine, but back then it

⁴ In 1986 the Gustaf Werner Institute was renamed The Svedberg Laboratory, after Nobel laureate The Svedberg.

⁵ As it happened, almost at the same time a French scientist, D. Comar, independently published the same finding in another scientific journal.

The hot cell is the part of the laboratory where the synthesis of the tracer takes place. The hot cell is shielded with a thick layer of lead to protect the researchers from radioactivity.

was somewhat of a revolution (interview Gunnar Antoni, 2011). In Uppsala most PhD students in radio chemistry would be working exclusively on chemistry development rather than creating and testing new tracer molecules. There was only very little pre-clinical experimenting going on and basically no clinical experiments at all. As time passed however, the focus of PET research began to shift, and chemistry gradually became more of research tool than a research topic. This means that the focus nowadays is on pre-clinical experiments, in which researchers try to evaluate if they can create any useful and interesting molecules, and later test them on animals or in vitro. There is also much research devoted to clinical applications of PET. In other words, it is more common for PET researchers today to have a biological goal with their studies, since the methods and chemistry needed are simply already there. Every now and then little novelties in methodology are introduced, but not to the extent as was the case in the 1970's, through the 1980's and well into the 1990's. A significant number of the most high-impact methods to synthesize tracers have originated from Bengt Långström and his research group (including twenty-eight PhD students over the years) at Uppsala. Essentially, this is what made Långström famous in the world of PET, and also how PET research at Uppsala University gained its renown.

The establishment of the Uppsala PET center

As time went by Långström began to express the need for a proper center dedicated exclusively to PET research, where the researchers would be given the equipment and facilities necessary for the experiments they wanted to run. Långström managed to rally support among distinguished figures at the university and at the research hospital in Uppsala, Uppsala university hospital. One of the people who along with Långström campaigned for the founding of a PET research center was Martin Holmdahl, who was the president of Uppsala university from 1978 to 1989. After some initial hesitation he became very enthusiastic and his support was instrumental in getting other influential people on board.

In the spring of 1989 the university and the Uppsala county council were discussing how a future PET center could be organized and how the two parties could collaborate to get the most out of PET. It was decided that the PET center would be a so-called "special institution", meaning it would reside directly under the university council and not belong to any of the other university faculties. The faculties which had an interest in PET research - primarily the faculties of medicine, pharmacy and science & technology - were supposed to contribute with some of their own funding to the PET center, meaning that they had the option of placing PhD students at the center. The fact that the PET center would not be part of any faculty had the consequence that it was not allotted any teaching hours, with the implication that no revenue could be brought in to the center from teaching university courses. Instead the PET center would have to finance its research activities by other means. It was agreed that one third of the financial resources needed to run the center would be covered by income generated from contract research, while the other third would come from external research funding bodies. The last third would be acquired by selling clinical PET services to Uppsala university hospital, i.e. the hospital agreed to use, and finance, a third of the center's capacity. Uppsala university signed an agreement where they committed to buying a total of eight hundred PET examinations per year, amounting to a value of 5 370 000 SEK (in 1989), or 6712,50 SEK per examination. This was the same price that researchers paid per examination, a benefit that was given to the hospital as the county council also agreed to build the house where the center would be located. The county council invested 10

^{7 &}quot;Särskild inrättning", according to ch. 16 in the university decree (Högskoleförordningen).

million SEK in the building, while the rest of the money required for the construction, about 40 million SEK, would be loaned by the county council. The university would then be the tenant and pay rent to the county council. The PET center project also received substantial contributions from various foundations, notably the Wallenberg foundation and the Söderberg's foundations, as well as the Pk-bank (what is today the Nordea bank). Along with these donations came a request from the some of the donors that the PET center be of assistance to other institutions in Sweden in need of PET. The funding nearly covered the cost for a cyclotron, a full-body PET scanner and a PET brain scanner. Still, to be able to start the center the university needed another 16 million SEK, money which had to be borrowed from the Academy Trust (Akademiförvaltningen)⁸ by Bengt Långström, the director of the PET center, and Martin Holmdahl, chairman of the board of the PET center. The interest for the loan was supposed be covered by the surplus the center was expected to generate. As it turned out, this surplus would never materialize.

PET center activities begin

After the decision to start the PET center had been reached two years passed before the operations actually started, as the building where the center would reside first had to be finished. In 1991 the center finally moved into the new facilities, which had been built in conjunction with another building on the premises of the university hospital. The infrastructure was now in place and the activities at the center could start.

Both Bengt Långström and Martin Holmdahl had an expansive network of relationships in the pharmaceutical industry, but despite these connections the center did not manage to land much contract research business during the first few years. Nevertheless, in the fall of 1992 the center signed a five year research agreement with a Japanese research institute which Långström had come into contact with through a Japanese colleague and friend. The goal of the Japanese research institute was to get access to the knowledge at the center through a collaboration project, for which the PET center was granted about 25 million SEK/year for a period of five years. The university was also supposed to contribute, but as they were allowed to count the investments they made when starting the PET center, they did not have to make any additional financial contribution. The research agreement ran from January 1993 to December 1997, and the funding the PET center received covered the financial needs as far as basic, non-contract, research went, and in addition made it possible to build a pre-clinical laboratory near the hospital. Culverts connected the PET center with the pre-clinical laboratory, enabling the researchers to transport tracers and other materials between the two locations without having to go outside. Two thirds of the laboratory belonged to the PET center and one third to the department of chemistry, which employed the PhD students who also worked in the lab. According to Långström these years were extraordinary; thanks to the new pre-clinical lab research was thriving and an abundance of new knowledge was generated.

At the same time the PET center was struggling financially. PET research is very cost-intensive, as the equipment is expensive to purchase and in addition requires skilled technicians to maintain it. As there simply was not enough money coming in to the center, the university had to cover part of the costs. And since financial resources tend to be scarce at a public university, not everyone at the faculties of medicine, pharmacology and science & technology was pleased that the PET center was receiving as much extra funding as it did. From July 1993 and onward, the three faculties were obliged to share the cost for one third of the yearly rent for the PET-center

⁸ The trust administers a number of foundations where the money is placed in stocks etc. and is loaned.

facility, as one third of the operations of the PET center was supposed to be dedicated to basic science, which the three faculties had an interest in. But the financial needs of the PET center was a sore issue, and for several years the faculty of pharmacology declined to make this payment. In the mid 1990's a deficit of about 28 million SEK had accumulated at the center and the university was worried. But in the middle of all this, in the fall of 1996, an international evaluation committee was invited by the university to carry out a scientific review of the PET center. In their report the delegation of professors praised the center for its outstanding research and infrastructure:

The PET-center at Uppsala University is one of international dimensions and is arguably the best in the world in the chemistry of carbon 11(...). The technical and scientific infrastructure has no equal elsewhere. This having been said, the power in collaboration and support for basic science facilities and general clinical efforts presents almost limitless possibilities. As such, these interactions need to be nurtured and supported. The University of Uppsala should be justly proud of having this unique facility in their midst. (p. 1) (...) With the respect to funding, the center's income which arises from the hospital, research grants and industrial collaboration is impressive. This is further underpinned by support from the University of Uppsala." $(p.2)^9$

In other words, there was no doubt that the PET center harbored excellent researchers and unique expertise, and for a university-run research facility it was bringing in an appreciable amount of money. The positive evaluation may have been a contributing factor to why efforts were made to keep the PET center running as before, despite the financial problems.

The use of PET at Uppsala university hospital

It was around this time that the hospital asked for a renegotiation regarding the clinical work at the PET center. Ever since the start of the center there had been a significant underuse in clinical PET examinations, i.e. the doctors were not using even close to the eight hundred examinations that the county council had committed to paying for every year. This was regarded as problematic. Part of the reason for this underutilization was that the number of patients was lower than expected, but also that the doctors felt they didn't have enough time to use the PET technique as much as had initially been the plan; for clinicians the use of PET was hard and timeconsuming work. Also, there were recurring complaints that the response time from the center, i.e. the time it took to get the PET scans interpreted and evaluated, was sometimes too long. These problems were addressed in meetings between representatives from the PET center, the university and the hospital, and a routine for how PET scan results would be efficiently communicated to clinicians was worked out. In addition, the parties also tried to solve the problem of the underuse of PET capacity by setting aside the part of the money that the county council had initially agreed to paid for PET examinations, and let these resources be used for clinical research projects. Clinical researchers would then be able to apply for funding from this pool of money, called "the Osterman quota" after Dr. Per-Olov Osterman who took the initiative to this solution. This initiative also happened to direct attention to what the international evaluation delegation had described as an area "requiring development", namely clinical research. As much as the PET center was commended by the international evaluation delegation for their research, it was also noted that "the status of the collaborations with clinical scientists is seen to fall short of that expected of such a formidable scientific and technical resource which the Uppsala University PET centre represents" (MRC scientific review).

⁹ Report, Medical Research Council, Clinical Sciences Centre, PET Methodology Group. November 1996.

Even though the hospital was not using the PET technique clinically as much as the parties had counted on, PET was still of vital importance to Uppsala university hospital. The department that depended on the technology most extensively both in clinical practice and for their research was that of endocrine oncology, which had made a name for itself as the most prominent unit of its kind in the world. The development of tracers suited for the investigation of endocrine tumors had started already in the 1980's at the university, and the fruit of that work was the tracer 5-HTP (5-hydroxytryptophan). The hospital, offering diagnostics and therapies for endocrine cancer, began attracting patients both from other parts of Sweden and abroad, meaning they were bringing in a much needed income to the university hospital. This is still the case today; the unique position of the department of oncological endocrinology and its use of 5-HTP still draw patients to Uppsala from all over the world.

The use of PET by the pharmaceutical industry

While finances were still looking bleak and the question of the deficit was a persistent theme, contract research was starting to take off. In 1999 the PET center signed a collaboration agreement with the contract research organization Quintiles, which functions as an intermediary between a pharmaceutical company wanting to have a pharmaceutical study carried out, and research institutes offering their services. For instance, in the testing of a new pharmaceutical Quintiles will gather groups of healthy volunteers and a PET center such as the one in Uppsala, will perform PET scans on the people involved in the study. The collaboration with Ouintiles generated a lot of of new business and toward the end of the 1990's contract research accounted for about two thirds of the revenues at the center. This is when the center started to "outgrow its suit", according to Långström (interview, 2011). Apart from the fact that the center was not breaking even, everything looked bright; scientifically the center was blooming and contract research was going so well that new researchers were hired. For Långström the next logical move was to step it up a notch and expand the center even further so as to be able to take on more contract research business, which, so the thinking went, would in turn finance even more independent research. The dream was a new spacious research facility, large enough to accommodate the growing number of employees, a new cyclotron and new scanners. The only problem was: money. Where would it come from?

Solution: commercialization

The PET center representatives and the university management agreed that the resources the PET center needed in order to operate the way the leading researchers wanted could not be provided by the university. As a consequence thoughts of commercialization started to arise, and in 2000 the university began looking into different commercialization alternatives; two consultancy reports were produced suggesting the entire center be turned into a business. The idea of housing not only clinical services and contract research within a commercialized PET center, but academic science as well, was met with resistance by some at the university. Nevertheless, eventually this was the model that was adopted.

II. The Uppsala PET center - The business years, 2002-2010. Owner: Amersham/GE Healthcare

As the Uppsala PET center had an excellent reputation it was not difficult to attract prospect buyers. Of the handful of biotech companies that showed an interest the choice fell on the British biotech company Amersham. At Amersham there was a strong conviction that having a PET center of their own would be of great benefit to the division Medical diagnostics, which specialized in contract solution. The university had a positive experience from previous collaboration with the other division of the company, Amersham Life Sciences, and believed Amersham was well suited to take over the ownership of the PET center. Amersham had formed a new company based on PET called IMANET (Imaging Network), which consisted of a large PET center at Hammersmith hospital in London, as well as a smaller PET center in Turku, Finland, and it was this company the Uppsala PET center would be a part of. Since Swedish legislation forbids an academic institution to take financial risks or make a profit on commercial ventures, the university was represented by its holding company UUAB in the negotiations. The part of the discussions that concerned the financial valuation of the PET center and ownership shares went smoothly; the university, or technically UUAB, would own 25% of the newly formed company, a share that was set to amount to a value of 50 million SEK. Amersham agreed to keep the academic research and later spin off the clinical operations and let the hospital be in charge of it, and also expand the contract research operations. In addition, the university insisted that Amersham put 45 million SEK into a research fund to be used for life science projects, which Amersham agreed to do. Issues that caused more lengthy discussions were those concerning the transfer of staff and equipment. The step into the commercial arena meant that the salaries of the employees at the center needed to match those of the rest of the industry, which eventually resulted in an increase in salary of about 30-40% for certain specialists at the center. The nurses on the other hand received only a yearly adjustment, which was a great disappointment to them. Working out this part of the contract took time, mainly because retrieving all the necessary information Amersham needed to make a correct business plan, was a time-consuming and arduous enterprise. But after a full year of negotiations, Amersham and Uppsala university signed the contracts on April 29, 2002.

A key point in Amersham's business plan for the PET center was to raise prices for both contract research studies and clinical PET examinations. After the increase the hospital had to pay the cost price for a PET examination, which turned out to be more than twice of what they had been paying up until that point, and the change in price applied regardless of whether the examinations were used for clinical work with patients or were needed for research purposes. As for contract research studies the prices doubled, but Amersham believed that the excellent reputation of the PET center and its established relations with large pharmaceutical companies would make the industry accept the new price list. As it turned out, this strategy only worked to a certain degree and for a limited period of time. At the time of the implementation of the new business plan the use of personal contacts and relationships was still the most important way for the pharmaceutical industry to find collaboration partners for a PET study. With its strong connections with the industry, the PET center benefited from this order of things and continued for a while to get business despite the dramatic increase in price and even though some of the companies they worked with questioned the pricing. But during the two years that followed the pharmaceutical industry started to formalize their routines for finding suitable PET centers to collaborate with; instead on relying on contacts they began sending out procurement proposals to the PET centers, choosing the center which could conduct the study to the lowest price, provided it also had the right competence at its disposal. Although the Uppsala PET center was still well regarded for its research, the fact that they charged more than any other PET center gradually

made them less attractive as a collaboration partner.

The take-over by Amersham involved a rise in costs at the PET center due to the increase of salaries and the establishment of certain administrative functions that had not existed previously. In addition, internal resources, which the researchers viewed as free of charge and had used as such while the university owned the center, were now regarded as carrying a cost that needed to be covered by external funding. For instance, laboratory animals were no longer "covered by the budget" and possible to use "for free" in experiments, but instead had to be paid for. This created tension between management and researchers at the center, who were not used to this logic and disliked how it hindered basic research.

The new commercial logic also changed the nature of communication between the hospital and the PET center. Contact which previously had been informal and direct became formalized; where doctors before had been able to simply call the center and ask that a certain tracer be produced, the new system required letters of referral and the response time could be long. Sometimes it would take months to get the desired tracer. Similarly, running tests on patients as part of clinical PET research projects became more complicated as the projects now had do be approved by a committee with representatives from Amersham instead of just being accepted by Långström at the center, as had been the case before. The new system was by medical researchers perceived as more stiff and bureaucratic.

At the same time as basic research was gradually weakening it also became obvious that the center was not going to be used within Amersham for the company's own research projects. Wondering how the PET center could really be of use to Amersham, the researchers busied themselves mainly with contract research projects which were now the focus of the operations. When it was announced that GE Healthcare had acquired Amersham it came as a complete surprise for the hospital and the university.

GE Healthcare enters the scene

Only two years after Amersham had purchased the PET center the organization now faced a new owner. With GE managing IMANET the emphasis on cost efficiency became even more pronounced; the first major measure was to let almost a third of the staff go, and the possibility to conduct basic science was hampered even further. A large primate laboratory that belonged to the university was closed down, much to the researchers' dismay. The fact that the PET center was not making a profit was now a serious problem; where Amersham's ambition for the center at first had been to merely break even—a difficult enough task — it was soon supposed to make a profit, an expectation which became even more accentuated when GE Healthcare took over. But except for in year 2006, where the center brought in a considerable chunk of contract research business and thereby managed to almost break even, contract business was waning, and it became increasingly obvious that GE considered the PET center to be a burden. The university, through the holding company UUAB, still owned 25% of the center but had a difficult time exerting any influence on strategy and operations. When UUAB sold all their shares in 2006, a sale that yielded 50 million SEK which were channeled into other academic commercialization ventures at UUAB, the university lost their seat on the board of IMANET and consequently whatever chance may have remained to have any impact on the way the PET center was run. Nevertheless, the university still had an interest in the PET center and together with the hospital it approached GE Healthcare on a few occasions to learn about what was going wrong at the

center and what could be done to improve the situtation. Eventually, in 2008, after four years of trying to turn the PET center into a profitable part of IMANET, GE Healthcare decided to sell. Knowing how critical access to PET was to the university hospital, GE contacted the county council to see if they were interested in purchasing the center. And as the scenario of having no PET center in Uppsala was simply inconceivable to the hospital there was no other option than to sit down and start negotiating with GE.

III. The Uppsala PET center -The hospital years, 2010-Owner: Uppsala county council

While the county council had already decided to purchase the clinical part of the PET center – although the details regarding the contract remained to be discussed – there was some uncertainty as to what would happen to the pre-clinical operations. As far as the county council was concerned the pre-clinical part was not interesting, and thus there were in reality only two alternatives; either to shut it down or for the university to take it back. Eventually the latter happened, meaning there were now three parties engaged in parallel negotiations. While the negotiations between the county council and the university were rather frictionless, the discussions which involved GE were more time-consuming, mainly because every decision and item on the contract needed to be be firmly established with headquarters in the U.S.

One of the most difficult issues to solve concerned tracers for which GE had patents. To be able to use these tracers for research in a lawful manner Uppsala university needed to obtain a so-called right to use license (RTU). However, GE was only willing to grant the university the right to use license for basic research, but refusing to let the center buy the license to use the tracers for contract research. For the university this question was a deal breaker; if they were not given the right to buy the license for all types of uses of the tracer, no contracts would be signed. It took quite some time for GE to reach a decision, since the information had to pass through the entire organization, all the way up to top management via the patent and the financial divisions. In other words, there was a substantial amount of bureaucracy, which caused a good deal of frustration among the negotiating parties in Uppsala. The issue was eventually resolved by adjusting the price of the license, making it more expensive to use it for contract research than basic research.

Another issue concerned the so-called "guarantee sum", a yearly payment GE would make to the PET center for a fixed number of years that covered about a third of the annual running costs. For this sum GE would get to purchase services from the PET center, the cost of which would be deducted from the guarantee payment. If the entire sum was not all used up, GE would have the right to conduct contract research at the PET center and keep whatever revenues that amounted to the remainder of the guarantee sum. GE had namely retrieved exclusive rights to carry out contract research where experiments were run on humans, while the PET center now only had the right to do contract research studies where animal experiments were used. Thus, on the one hand the PET center will have a guaranteed inflow of money through the payment GE makes every year, on the other hand they will not have the opportunity to carry out lucrative clinical contract research studies. As disadvantageous as some perceived this part of the contract to be, the county council felt they really did not have much choice but to accept the offer given how restricted their own finances were.

It took two years, including a six month time-out needed by the county council to think it all over, for the parties to reach an agreement and sign the contracts. In the late fall of 2010 the PET center returned to public ownership, but so far the hospital's access to the PET center has not improved. Since the PET center receives part of its funding from GE via the guarantee sum agreement, the researchers are much engaged in projects with their former owners. The consequence has been that the waiting time to get a PET examination done is still as long as it was before the hospital took over, as the equipment is often being used in projects related to GE. Furthermore, there is still a long wait to get the tracer 5-HTP produced, since the cyclotron is usually being used to produce FDG for other projects. The time it takes to get the PET images analyzed has however decreased since the hospitals now has a doctor specialized in nuclear medicine.

As the transfer of the PET center from GE to the county council is so recent the effects of the new ownership have most likely not yet appeared in full, and only time will tell if the expectations of the hospital of a facilitated clinical use will come true, and if pre-clinical research will gain new momentum.

Analysis

Since this is a work in progress neither the empirics nor the analysis has taken a distinct shape, but in the following section I will discuss the empirical findings made so far by using the 4R model and applying it in three different settings: the producing, developing and using settings. I aim to take a closer look at some of the resource interfaces in the network surrounding the PET center to understand the journey that the center has been through.

A grasp of the parts that make up the PET technique is key to better understand the commercialization, and subsequent de-commercialization process of the Uppsala PET center, because it is partly the complexity of the technique that has caused and necessitated interaction within the network. For this reason the PET technology will be central to my analysis of the commercialization journey; a special focus will be placed on the radio tracers as they, so to speak, are the least common denominator for all the actors with an interest in PET; the tracers are the resource the PET center at Uppsala both develops, uses and produces. Moreover, the tracers are a resource necessary to carry out studies for the pharmaceutical industry, and one that the university research hospital is dependent upon. In other words, the production, development and use and of tracers are in a sense what unite the three main actors in this case study – the university, the hospital and industry.

The using, developing and producing settings

At the PET center in Uppsala the resources used, actors involved and activities performed in the use, development and production of PET are very similar regardless of setting. This does not mean that the three settings are indistinguishable, but simply that they often intermingle.

The producing setting

At the heart of the productive output at the PET center is the radio tracer, a principal ingredient in a PET examination. The reason tracers are so central is not that they are the only necessary resource in PET – scanners and cyclotrons are just as indispensable – but what sets tracers apart is the fact that this is what the research activities at the PET center revolves around; the main

occupation of PET researchers is to develop new tracers. Furthermore, it is the tracer that determines exactly what is going to be examined with the PET scanner. As explained before, tracers come in many variations, and their use depends on their specific chemical constitution. For instance, one tracer may be designed to study a certain brain pathology while another one will show us where in the body there is a tumor. In that way the tracer sets the course for the PET examination.

Mixed interfaces between the PET technique and the "products" of the PET center

Now, as described in the empirical sections, PET examinations are used for a few different purposes. First there is the independent basic pre-clinical research, which, as mentioned above, is centered around the development of new tracers. Then there is contract research, where pharmaceutical companies, sometimes mediated by a contract research organization e.g. Quintiles, pay the center to help them carry out scientific studies, usually related to the development of pharmaceuticals. Thirdly, PET examinations are used in clinical research and in clinical practice. In other words, it is possible to divide the PET center into three different producing settings: independent scientific research as a producing setting, where the output is academic publications in which research findings are presented; contract research as a producing setting, where contract research studies are produced, and where the results are used by the pharmaceutical industry in the development of pharmaceuticals and sometimes published in scientific journals by the researchers; and finally healthcare as a producing setting, where PET examinations are produced for the hospital. In addition, there is a minimal production of the FDG tracer that is sold by the PET center to hospitals relatively close by. This will be described in the next section.

Mixed interfaces between the PET center and hospitals outside Uppsala

At the Uppsala PET center there is a marginal production of the tracer FDG (fluorodeoxyglucose) to cater to the needs of hospitals nearby. This production is of no commercial value to the PET center as the tracers are sold at a cost price as a "gesture of courtesy", in line with the wishes expressed by some of the center's donors (interview, Antoni 2010). As mentioned previously, some foundations donating funds to the center back in 1989, had asked the center be of use to hospitals in Sweden, and this is what the PET center is still trying to do. FDG contains a fluorine isotope with a half-life of two hours which makes it possible to ship to hospitals in regions not too far away. This is a long half-life compared to tracers with carbon isotopes, which has a half life of 20 minutes, or oxygen isotopes, where the half life is only 2 minutes. The relatively long half life and the widespread use of FDG in oncology makes it interesting to produce from a business point of view. Nevertheless, since the focus of the PET center is to carry out research and be of service to the university hospital, as opposed to produce and sell tracers in bulk to other hospitals, the major share of the tracers produced are used for PET examinations that take place at the center and at the university hospital.

Organizational interfaces between the PET center and its customers

The relationships between the main actors involved have proved to be very important resources. For instance, the five-year research agreement between the Japanese research institute and the PET center in the 1990's came about through Bengt Långström's personal connection with a Japanese scientist, and the fact that Långström was well-connected with important actors in the pharmaceutical industry also gave the PET center a considerable amount of business. The relationships between the PET center and the pharmaceutical industry were therefore tended to so as to generate more contract research. When Amersham came in as the new owner and launched their new business plan, which as mentioned above included a doubling or even tripling of prices for contract research studies, they were convinced that the renown of the PET center, and its well-established relations with the industry, would make the pharmaceutical companies accept the new price list. As explained previously, this did not work out in the end, but it goes to show to what an extent actors may attempt to use their relationships, or in this case somebody else's relationships, to achieve what they want. Other important relationships in the producing setting are those between the nurse at the center handling the planning of PET examinations, and the doctors, nurses and researchers at the hospital. Particularly during the time Amersham and GE were in charge of the center, but also now when the hospital has taken over and GE uses the center's equipment for its own research projects, a good informal relationship with the nurse enhances the hospital's chances of getting speedier access to the PET equipment.

Mixed interfaces between the PET technique, the hospital and the PET center

Dividing up the resource capacity between the different "products" at the PET center has not been a straight-forward undertaking. During the years of commercial ownership the "clinical production" of PET examinations, carried out for both clinical research and medical practice, at times tended to be squeezed out by contract research projects. In other words, the production of pharmaceutical studies was increasingly given precedence as Amersham, and later GE, took over as owners. Since the PET technique is the tool needed for both clinical PET examinations and for pharmaceutical studies, the same resources in terms of laboratory equipment and know-how are required for the two products. As a consequence, the use of resources in the producing setting has been surrounded by conflict, and still is, even after the county council became the owners of the center in late 2010. Issues have revolved around access to hot cells and the PET scanners, and around what kind of radionuclides should be produced in the cyclotron to produce certain types of tracers, and when. As we will see, this conflict over resources is not limited to the producing setting, but is present also in the developing and using settings, as the three settings overlap.

The developing setting

The setting in which production takes place is very similar to the developing setting; what the center produces is essentially the same thing as it develops, namely research. And what does not count as research per se, such as PET examinations sold to the university hospital (where the examinations are used for clinical research or as a tool in the work with patients), is based on research and may be used for research. Development takes place in both independent pre-clinical research activities and in clinical research, as well as, to varying degrees, in contract research where PET researchers may collaborate with scientists from the pharmaceutical industry ¹⁰.

¹⁰ Of course, from the perspective of the pharmaceutical companies for which the Uppsala PET center conducts studies, contract research is always an important part of the development work. For the PET center however, these studies don't always necessarily develop PET research.

Organizational interface between the PET center and the pharmaceutical industry

The relationship between the researchers at the PET center and the pharmaceutical industry has been one of mutual dependence. Pharmaceutical companies need the knowledge of the researcher to be able to conduct the studies necessary for the development of pharmaceuticals, but the researchers at the center also need the knowledge at the pharmaceutical companies to develop new tracers. While some tracers consist of natural chemicals such as water and ammonium tagged with a radionuclide, they may also be made up of a molecular structure which is modeled after a pharmaceutical drug. Even though there certainly is pharmacological competence at Uppsala university – the department of medicinal chemistry is the main collaborator for radio chemistry and pre-clinical PET research since the sale from GE – the PET center has often relied on the pharmaceutical industry to learn about the molecular bases needed to develop new tracers. The pharmaceutical molecular structures are usually obtained from scientific journals, as such scientific findings may be published as long as it does not disturb pharmaceutical development or patenting processes, but may also be attained simply by looking up the content of pharmaceuticals that are already registered. One element in Amersham's strategy towards the pharmaceutical industry was that pharmaceutical companies would make their IP rights regarding molecular structures available to the PET center when purchasing contract studies from the center. Contract research was thus expected to yield more than just revenue; when developing a new molecule together with pharmaceutical companies Amersham expected the collaborating company to agree to sell the IP for the molecule to the center, which would then use it to advance PET research further, but also utilize it in contract research with other companies. Not surprisingly perhaps, the idea of sharing IP with the PET center under such conditions was not appreciated by the industry, meaning that this part of the plan was never realized.

Mixed interfaces between PET researchers and laboratory animals

The conditions for the developing setting (as well as for the producing and using setting) have changed as the ownership has been passed from the university to Amersham and GE Healthcare, and then back to the public sphere. This has affected what and how resources are used, as well as the interaction between the PET center and its collaborators. One issue which caused particular commotion at the PET center was the closing of the primate laboratory, which had belonged to the university for a long time. As the use of monkeys in research experiments is a highly sensitive matter, the primate laboratory had been receiving some negative – but also positive 11 – attention over the years. Even though the monkeys were not experimented on on a daily basis, the laboratory was readily available when a monkey was needed. Running this laboratory was quite expensive; the center paid a yearly cost of 6 million SEK. Soon after GE Healthcare took over a decision was taken to close down the primate lab, both for economic reasons and because GE did not want to own a facility that could attract the attention from animal rights activists. Since the primate laboratory was a critical research resource at the center the researchers were not happy about it being shut down, although the large costs – about 5,5 million SEK per year – were difficult to defend. But as it happened, one of the researchers had a contact at the Swedish Institute for Communicable Disease Control (Smittskyddsinstitutet), and it was determined that the PET researchers would be able to rent monkeys at the institute to a cost that amounted to about a tenth of what they had been paying for the primate lab. Thus, monkeys as a resource for

¹¹ At one point the facility where the monkeys lived was awarded a prize from an animal's rights organization for good living conditions.

experiments was secured. Nevertheless, from having been available for both basic independent research – there were for instance PhD theses written based on experiments on primates – as well as contract research, the costly use of monkeys was now limited to contract research only. The use of other test animals e.g. pigs and rabbits was likewise cut down. We can thus see a shift in the use of laboratory animals, as lowering of costs became a priority for the owners of the financially weak PET center. The effect of this restriction on basic research at the center was detrimental.

Organizational interfaces between the PET center and the business strategy of Amersham/GE Healthcare

The transformation of the PET center from a university-owned place of research to a company expected to be profitable, meant that the focus on what kind of development should be taking place changed. While quite a large amount of contract research had been conducted at the center during the end of the 1990's and the first year of the new millennium, i.e. already before commercialization took place, the acquisition by Amersham, and later by GE Healthcare, brought about a change in the division between contract research and basic research, where more emphasis was put on the former at the expense of the latter. As a part of GE Healthcare's strategy to cut costs and increase revenue came the decision to let on third of the staff at the PET center go; the consequence was that several accomplished researchers had to leave their positions at the center. All in all, this restructuring and shift in priorities in regard to research activities changed the developing setting in basic research profoundly. Whereas the researchers had believed that commercialization would vield *more* resources to be used for independent basic research, it turned out that quite the opposite happened. What made sense to the researchers was to engage in as much interesting research as possible, while at the same time make their expertise useful to their owner. However, what made sense to the owner was to run a business in such a way that as much revenue as possible was made.

This clash between the logic of science and that of business permeates the story of the PET center from beginning to end and, as we will see, is visible also in the using setting.

The using setting

Who are the users of Uppsala PET center? If by the PET center is meant the collected set of equipment, tracers and knowledge, the major user groups are the ones which have been discussed in preceding sections, i.e. the hospital, the pharmaceutical industry and researchers. As mentioned previously there is also a minor user group made up of hospitals in nearby regions to whom the PET center supply small amounts of the tracer FDG. In that case the center's function is more that of a "tracer factory", where the center merely manufactures the needed tracer as opposed to providing full PET examinations. There has also been another research group, belonging to a GE-owned research company, renting part of the pre-clinical laboratory and the equipment there off and on, thereby engendering some income to the center. In other words, the PET center is employed for various purposes, the main users being the university hospital, the pharmaceutical industry and researchers.

Mixed interfaces between the PET center and the users

For the pre-clinical researchers at the PET center, to use PET is to develop it further, which, as explained above, is done through independent research, as well as to some extent through contract research. In addition, academic researchers also use their research to promote their

careers by publishing in scientific journals. Naturally, the research emanating from the center is used by other researchers in the field too to generate new knowledge. Rather than focusing on tracer development, clinical researchers apply the technique to study different medical conditions and response to treatments, while physicians use PET to diagnose their patients and monitor the effect of treatments and therapies. Finally, the pharmaceutical industry uses the collection of resources available at the center, including the researchers' scientific knowledge and expertise in making tracers, as well as its knowledge in running the equipment, and of course the equipment itself, to develop new pharmaceuticals.

Mixed interfaces between tracers, contract research, and the hospital

For all these users the tracer plays a decisive role; as mentioned before it is the particular type of tracer that decides what kind of research experiments can be carried out, what part of the body that can be investigated, and what pharmaceutical drug that may be studied. Consequently, what tracers are needed depends on what type of examination is going to be performed. As touched upon above the division of time and resources between the different examinations and users has not been evident; notably, there has at times been a collision between the university hospital and contract research activities. The major user of PET at the university hospital is, as mentioned previously, the department of oncological endocrinology where the the carbon 11-labeled tracer 5-HTP is used to investigate endocrine tumors. The tracer used for this type of tumor is the carbon 11-labeled 5-HTP (5-hydroxytryptophan), the synthesis of which is so complex that it is only at the PET center, the place where the tracer and method to produce it originated, where there are researchers with the skill to complete it. Furthermore, as the half life of the carbon 11 isotope is only 20 minutes it has to be produced in absolute vicinity of the hospital; there are thus two reasons why the hospital depends fully on the PET center for the supply of 5-HTP. This dependence did not pose much problem during the years when the university owned the center as the 5-HTP could be produced with short notice whenever the hospital announced their needs. The acquisition by Amersham and GE was however frustrating for the hospital, since, as explained above, contract research tended to come first, while the clinical use of PET came second. In many contract research studies it is mainly the fluorine-based tracer FDG that is used, which requires that the cyclotron be used for the production of fluorine-18 isotopes. With the cyclotron thus often busy making primarily fluorine-18 isotopes, the hospital would oftentimes face long and occasionally unexpected waits. As pointed out above, this is still the case even after the county council's purchase of the PET center, since the center is still greatly involved in contract research and services related to GE.

Mixed interfaces between PET examinations and the hospital

A waiting time that bothered some physicians at the hospital both during the years when the university owned the center and during the eight years that followed after Amersham's acquisition, was that to get a PET examination. At the same time, one researcher at the center expressed the view that the severity of the troubles experienced by the hospital was relative, as it takes months to get an MRI scan or a new knee meniscus at any hospital in Sweden. The question of waiting time for a PET scan thus having varying gravity depending on who you ask, doctors wish for quicker access; as of now the hospital has not noticed a major change for the better as far as availability of PET equipment is concerned, waits for PET examinations are still long, particularly when 5-HTP is required, as contract research and clinical use still compete over resources. Nevertheless, this may of course change as the hospital settles in as the new main owner of the PET center.

The hospital was in the past also concerned about the amount of time it usually took to get the PET images from an examination interpreted; since the PET center lacked a radiologist of their own the scans had to be sent to a radiologist outside of the PET center, often resulting in a long response time. This has been especially problematic for the endocrine patients that have come from abroad for PET examinations and wanted the results before going back home. After the hospital's purchase of the center, the problem seems however to have been solved by the hiring of a doctor specialized in nuclear medicine.

Organizational interfaces between the PET users and Amersham's/GE's business strategy The commercial ownership was problematic for the hospital not only because of the increased waiting time to get certain tracers, but also because of the dramatic increase in prices for PET examinations it involved. After the increase the hospital had to pay more than twice as much for a PET examination, irrespective of whether the examinations were used clinically with patients or needed for research purposes.

As mentioned previously, the new price strategy affected the pharmaceutical industry as well since the price for pharmaceutical studies also doubled, resulting in a gradually shrinking amount of contract research business. Also, the strategy to reduce academic research at the PET center to make room for lucrative contract research eventually backfired somewhat; for a PET center to remain interesting to the industry as a scientific collaboration partner, it has to maintain a research edge, produce academic research and publish. Thus, as the time and resources to carry out academic research were seriously circumscribed, the center lost some of its earlier appeal. Another possible for reason for the decreasing contract research business, suggested by the researcher who has been in charge of contract research at the Uppsala PET center for many years, may be found in the restructuring of the pharmaceutical industry. Several large mergers have reduced the number of pharmaceutical companies and, as a consequence, the number of potential individual customers wishing to use PET technology.

In the case of Uppsala PET center we thus see that during the years of commercial ownership, the pharmaceutical industry's use of the PET center was affected by both changes within the pharmaceutical industry, manifested in the new formalized procurement routines described in the empirical section, and a reduction in the number of companies, as well as by the aggressive business strategy adopted by Amersham and GE Healthcare.

Conclusion

Despite the failed attempt to turn the PET center in Uppsala into a profitable company, the center has since its start created some highly successful innovations. Well before the actual center was founded, Långström developed methods to synthesize tracers, and thereby revolutionized PET research as other researchers started to employ these methods to produce new tracers. The development of tracers at Uppsala university was very fruitful, and apart from being used in research, the tracers were used extensively at the university hospital and in the pharmaceutical industry for whom the PET center conducted studies, sometimes using their own tracers or tracers developed in collaboration with the industry. In other words, the PET center has been a strong innovative force, cooperating with both the hospital and pharmaceutical companies long

before commercialization took place. Thus, as far as usefulness goes any innovation policy-maker would be content with what the PET center has achieved. Why then is this not a story of success?

As a university research center with great ambitions and a need for very costly research equipment, the PET center started facing serious financial problems early on. As the contract research the center conducted to finance its operations was not enough to cover the rapidly accumulating deficit, the center came to largely depend on the university for its survival. Given the economic circumstances the university management and many researchers at the center agreed that commercialization was the best way to ensure a prospering future for PET research in Uppsala, especially since Långström's wish was to expand the PET center to make room for even more contract research and basic science. Amersham appeared on the scene, contracts were signed and the work began. This is where the fundamental clash of expectations soon became obvious. From the viewpoint of the university, the sale had appeared as the best solution available to free themselves of the financial strain that the responsibility for the PET-research entailed, and simultaneously the best way to make sure that the needs of the center were met. The PET researchers' paramount interest was to get access to new physical resources, including a new PET building, a new laboratory, a new cyclotron and state-of-the-art PET scanners, which would enable them to keep on producing excellent research. While certainly interested in the scientific role PET could play for research conducted within their company, Amersham at the same time had a strong interest in the direct economic value that they expected to be able to generate from the PET center. When GE Healthcare took over the emphasis on profit became even more pronounced, and since the annual accounts were never satisfactory the Uppsala PET center soon turned into a burden. At the same time the economic value of the center to the hospital remained unchanged. This points to the heterogeneity of the PET center as a whole; the way the center had been organized at the outset made little sense from a business perspective, which is why GE struggled to increase revenue by focusing on contract research and cutting down on basic research. The hospital on the other hand had depended on the center since its start to be able to offer the full range of health care that should be available at a university hospital. With patients coming from other counties in Sweden as well as other countries to receive care involving PET examinations, the hospital was earning a much needed income which would not have been possible without access to the PET center. The heterogeneity of resources is discernible on a "micro-level" as well, as in the case of 5-HTP, the tracer which could only be produced at the PET center in Uppsala. To Amersham and GE the production of 5-HTP was not very interesting from a commercial point of view since it was not used much in contract research. Nevertheless, this tracer was of crucial importance to the department of oncological endocrinology as they used it both in research and to diagnose and treat patients from all over the world.

During the years of commercial ownership the researchers at the center were wondering why they were not asked to collaborate with researchers at Amersham/GE, as opposed to just carrying out contract research which at any rate was not bringing in enough revenue. Instead of creating value by engaging in research projects at the mother company, much like a regular R&D division, the PET center was expected to generate economic value only through contract research. It appears as if important interfaces, both physical and organizational ones, between the PET center and the researchers at Amersham/GE were missing, leaving the center to operate alone, more or less cut off from the rest of the company. It was not until the very end, when the decision to sell the PET center had already been taken, that GE Healthcare actually started using

the competence at the PET center for their own projects. This use is planned to continue to some degree even now when the university hospital runs the center, as the so-called guarantee sum that GE pays every year gives them the right to buy services, the cost of which is deducted from the yearly payment. It is this use, along with the pure contract research projects, which at times has been in conflict with the hospital's use. In other words, the activities that create business value for GE at the same time obstruct the interface between the hospital and the PET technique. But to complicate the situation even further the county council and the hospital are dependent on the guarantee sum, and hence the presence of GE, to run the center at all.

And what about the independent basic science? From the perspective of the scientific community, where careers are advanced and research grants awarded based on the number and the quality of a researcher's publications, reducing the quantity of basic research means reducing the chances of getting academic recognition and funding for future projects. Even though contract research studies too can yield publications, independent basic science has a greater chance of doing so as anything that the researchers want to publish may be published. And importantly, the researchers themselves choose what to study.

The idea of what commercialization would bring to the PET center was bright and optimistic; it would be a way to expand a highly regarded research center, keep up scientific excellence, produce new cutting edge research, yield commercially successful innovations in collaboration with pharmaceutical companies and bring in a profit for their owners. Clearly, commercialization meant one thing for the university and quite another for the buying company, and the failure to marry the logics of science with that of business eventually resulted in the PET center coming full circle, i.e becoming de-commercialized and returning to public ownership. With the single largest user now in charge it remains to be seen which direction the journey of the center will take.

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