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The Patterns Venture Capital Investment in the UK Bio-Healthcare Sector: the Role of Proximity, Cumulative Learning and Specialisation

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Abstract

This paper focuses on the patterns of Venture Capital (VC) investment in dedicated biotech firms (DBFs) in the therapeutic and diagnostic sectors (bio-healthcare). We use a database of 655 UK bio-healthcare deals to map the geographical flows of VC investment and measure the co-location of investors and DBFs. Then, using 20 face-to-face interviews with venture capitalists (VCs) and DBF firms in Cambridge and Scotland, we study the strategic motives underlying the co-location of investors and investee companies and reflect on the catalytic role VCs play in context of the Scottish and Cambridge bio-clusters. From the viewpoint of VC-related policies, we find that our study is more in line with arguments stressing the attractive power of “investor-ready” opportunities (Mason and Harrison 2003) than supply-side approaches that take VC presence at the core of high-tech clusters for granted. In line with Avnimelech et al (2008), we propose that VC policy should be consistent with the wider strategic objectives innovation and technology policy.

Keywords: Intermediation; financing; venture capital; biotechnology; DBF; investor proximity; geography

1. Introductory notes: “Classic” and “Merchant” VC

VC originally recombined the role of scientists, investors, capitalists, entrepreneurs, and managers. In the US, the volume of VC investment accelerated in the 90’s, as fundraising grew thanks to increased investments by pension funds and large corporations (Gompers and Lerner, 2001). This growth ended with the stock market collapse of 2001 and the subsequent downturn had negative implications for early-stage ventures (OECD 2003). Thus, originally emerging as a quasi public intermediary to invest in technology-oriented firms with high growth potential, VCs have become increasingly oriented towards established businesses.

VCs oriented towards ventures at their seed, start-up and expansion stages, with principally knowledge-based assets, are referred to by Mason and Harrison (2002) as ‘classic’ VC. VCs that focus on later stages, including management buy-outs or buy-ins, are referred to as ‘merchant’ VC. In spite of the expansion of ‘merchant VC’, “classic” VC continues to be a catalyst of clustering dynamics in areas such as California and Massachusetts (Gompers and Lerner 2001) and a key component of the local infrastructure of innovation (Powell 2002). As Florida and Kenney (1988) put it, ‘classic’ VC represents a ‘third-way’ in the Schumpeterian dichotomy between corporate and entrepreneurial capitalism. VCs act as ‘technological gate-keepers’ which steer and direct companies towards those regions with the ideal mix of factors to promote innovation, such as Universities, R&D capabilities, and managerial skills.

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VC investment in bio-healthcare is motivated by the promise that the industrial application of molecular biology will lead to the discovery of new and better solutions for patient healthcare and the exploitation of large unmet opportunities. In spite of rather disappointing performances by both financial and operational measures, the business of bio-healthcare has maintained attractive to investors event throughout the 2001 downturn (Pisano 2006). Then, in the 2005/07 period R&D and financial performances improved both in the US and EU. In 2006, the pipelines of publicly traded EU DBFs grew by 30%, with around 700 new compounds in clinical trials, plus 27 compounds awaiting regulatory approval. Europe's privately held DBFs were estimated to have 800 drugs in their pipelines, and 12 compounds in registration. Revenues in 2006 increased by 13% to €13.3bn (compared to a 12% fall in 2003), market capitalisation increased by 43% to €62bn (Ernst & Young 2007).

In 2007, companies in the Americas and EU raised more than US\$29.9 billion, a new high excluding the outlier genomics bubble year of 2000. VC financing reached \$7.5 billion, global revenues of public biotech companies increased by 8% (amounting to \$80 billion) and the global industry's net loss decreased from \$7.4 billion in 2006 to US\$2.7 billion in 2007 (Ernst & Young 2008). Even in 2008, biotechnology continued to represent 28% of total investments (2nd largest sector). However, due to the current financial crisis year 2008 was one of the most negative for market capitalisation and IPOs. All forms of financing plunged in comparison with 2007 (<http://www.burrillandco.com/news-Biotech>) including VC investment that contracted by 15% (<https://www.pwcmoneytree.com>),

Worldwide, some locations have become epicentres of path-breaking research efforts in bioscience, with the ability to attract skilled people and risk capital (Cooke 2007). In this paper, we use both quantitative data and interview data to map the geographical flows of “classic” VC investment in UK bio-healthcare. We investigate why distinctive patterns of investment arise and evaluate the importance of co-location between investors and DBFs for determining the patterns observed. In so doing, we explore whether UK VCs play a catalytic role (Florida and Kenney 1988; Avnimelech and Teubal 2006) vis-à-vis bio-cluster emergence (Powell et al 2002; Niosi and Banik 2005; Cooke 2007).

2. Venture capital investment in biotechnology: Risks, opportunities and current trends

For many years the drug discovery method of Pharmaceutical Corporations (PCs) was referred to as random screening. Under this approach, large numbers of natural and chemically derived compounds are randomly screened in experiments for potential therapeutic activities. In spite of increasing R&D budgets and a drop in screening costs per compound (Northrup 2005), since the mid-80s this approach has been characterised by lower productivity and negligible economies of scale. Many practitioners now feel that an improved understanding of the biological basis of life allow for better and more informed choices before entering the development stage.

New discoveries in the domain of life sciences stem to a significant extent from publicly funded research. Thousands of DBFs, a significant proportion of which are spin-offs of university labs, have embarked on translating scientific advances into proprietary concepts and platforms that are used by PCs to fill emptying pipelines. Critical I (2006) reported the existence of 3806 biotech companies at varying stage of development: 150 of them (83 in the US and 67 in the EU) account for 44% of total

employees, 35% of the research effort and 60% of the revenues. From a geographical point of view, DBFs tend to proliferate in proximity of bioscience intensive areas, that is, locations characterised by a significant concentration of public and private research budgets, activities and infrastructures, medical hospitals and an array of intermediaries that can help remedy competence gaps (Audretsch and Stephan 1996; Cooke 2004 and 2007; Powell et al 2002; Rosiello 2008).

Overall, the main motivation for VCs to invest is an expectation of enormous returns, Northrup (2005) estimates that given opportunities to cure disease the pharmaceutical market is potentially worth \$1.6 trillion. From an investor's viewpoint, however, drug R&D is perceived as long-term, capital intensive and uncertain. Indeed, because of the rapid pace of innovation, the uncertainty and complexity of both the technological solutions and the underlying science, and the high costs of clinical trials, the chances of a drug candidate going through concept development, regulatory approval and commercialisation remain low.

Technological uncertainty relates to fundamental questions about technical feasibility. The industrial application of molecular biology entails an in-depth understanding of the biological processes of disease. At the same time, drug development requires major investments throughout all stages of basic research, drug development, clinical trials, regulatory approval and large scale distribution of the product. Regulatory uncertainty is primarily caused by the low probability that a product receives approval from a competent body. The extreme case is that of drug discovery where regulatory approval includes approval of pre-clinical screens, reports of all clinical tests, and other aspects of preclinical process, and product development. The entire discovery-development process may take between 10 to 17 years.

Another source of uncertainty is price regulation. Differences exist among countries. In the US, personal insurances tend to induce cost-conscious behaviour by prescribing doctors (McKelvey and Orsenigo, 2001). In most European countries, governments exercise forms of direct and indirect control. In the UK, caps are defined in relation to the overall rate of return. The margin is negotiated by each firm with the Department of Health which receives advice by the National Institute of Clinical Excellence that employs cost-benefit analysis to decide which treatments should be made available through the NHS, causing additional delays and uncertainty.

Some legislation is aimed to reduce uncertainty, time to market and R&D costs. A classical example is the Orphan Drug Law ratified by the US Congress in 1983 and providing companies with 7 years exclusivity on new products as well as mechanisms for quicker approval. More recently fast track drug development programs have introduced to facilitate the development of life-threatening diseases, like cancer.

3. On intermediation, risk management and added-value

The risk profile of many DBFs is such that most financial institutions (especially in Europe) are not inclined to supply loans or other forms of finance. VC can be a solution, but various problems remain. Firstly, DBFs tend to lack tangible assets required as collateral to obtain finance. Secondly, investees often use the money raised to support transaction-specific activities, which increases the risk of non-redeployability in the case of failure. Thirdly, business development is affected by high attrition rates, changing regulation, and high financial requirements. Finally, investors face information asymmetries, in that entrepreneurs are generally better informed about the prospect to achieve a successful exit than VCs.

The economic literature has mainly portrayed VC as a financial intermediary able to lessen transaction costs and deal with information asymmetries (Gompers and Lerner 2001). This function seems important especially in the presence of complex processes and uncertain conditions. For example, Gompers and Lerner (2001) explicitly refer to situations where the management team of a DBF either over-invests in basic research or raises unsustainable amounts of debt. When the contracting parties are linked by bilateral dependency, as in the case of VCs and investee DBFs, distortion of information and non-disclosure may arise. Thus, according to Pisano (2006, 136), in the context of biotech, VC “needs to be understood as both a source of funding and as a mode of corporate governance. VCs do not just provide money; their investment comes with close oversight”.

However, DBFs frequently need not only money, but also active management support and advice. In that respect, the “added-value” approach to VC lays emphasis on the provision of strategic advice and management support in terms of capabilities and network of contacts that contribute to business development. Depending on circumstances, VCs are viewed as knowledge reservoirs (Zook, 2004), coaches (Hellmann and Puri, 2002) or certification providers (Hsu 2004). Such functions seem particularly important in locations where serial entrepreneurs and experienced managers are in short supply, and companies are typically started-up by research scientists who lack business acumen.

VCs can provide assistance to recruit senior managers and, at times, replace the scientific founders with experienced managing and financial directors. The VCs’ investment decisions are “based on opinions, projections, and conjecture, which may be extremely difficult to codify”, in some cases on “gut feelings about the people involved” (Zook 2004, 634). As a result, VCs gather information to assess the risk associated with specific investments via professional and personal networks. Once the company has been selected, VCs will be able to use the same network to support their investees and protect their investment. Hsu (2004) claims that investees are willing to offer a 10-14% discount in the share-holding agreement to high-reputation VCs.

4. On intermediation and locational choices

4.1. Scouting, assessing and monitoring

Various sources, including Powell et al (2002), Porter et al (2005), Cooke (2007), Critical I (2006) and www.pwcmoneytree.com, suggest that VC investment in bio-healthcare is concentrated (especially in the US) only in a few regions. Such concentration is due to the fact that research and capital intensive industries, such as biotechnology, shape the firm’s tendency to locate in close proximity to public research laboratories and universities, generating bio-clusters which exhibit a variety of network and knowledge externalities (Cooke 2004). From an investor viewpoint, being located in these areas means that selecting and screening good opportunities can be more easily accomplished nearby world-class bioscience (Orsenigo 2006), ‘star’ scientists (Audretsch and Stephen 1996) and a high number of DBFs.

First, proximity facilitates face-to-face interaction and the transfer of vital information – know-what (Florida and Smith 1990). Second, most investments are referred deals, meaning that VCs are more likely to invest in business opportunities that come up from people they know and trust (Zook 2004). To sustain a steady flow of referred deals, VCs need to invest in social capital. Social capital tends to originate from the intersection of weak ties (Granovetter 1973), social and professional

relationships and attendance at various events. Further, reputation and trust take time to develop and are the normally the result of long-term working relationships. This is clearly the case of business angels (BAs) who tend to invest in local companies, build their reputation and network in the location where they operate, and use this network to value to co-located investees (Madill et al 2005).

Third, proximity is important for monitoring. VCs take seats on the board of directors either directly or by appointing non-executive directors that they trust. Some advisors and non-executive directors spend a considerable amount of time in direct contact with companies and are habitually located nearby. If the investment is made at a long distance or in places where VCs lack contacts, problems may arise in finding non-executive directors and advisors and/or communicating with them (Zook 2004).

4.2. Adding-value

The added-value argument appears particularly salient in bio-healthcare, a sector that entails an intrinsically high technological and regulatory uncertainty in front of long times of realisation and high capital requirements. The transfer of added-value by VCs coincides with the absorption and development of capabilities and contacts that may not be available internally, but are vital to develop and commercialise new technology and products. Hence, the relationship with VCs may be essential not only to raise money, but also to promote inter-organisational learning and growth.

Many new DBFs are built upon relevant scientific expertise and intellectual property (IP). These assets are distributed across a number of centres of excellence worldwide. However, only some of such centres of excellence have been able to exploit them commercially at a large scale (Cooke 2007). This may be due to the absence of the necessary infrastructure for innovation, encompassing an array of market and non market mechanisms for knowledge creation, transfer and exploitation.

According to Powell et al (2002, 196), in biotechnology VCs provide “more than just money”. Since most founders of DBFs are scientists with little business acumen and managerial experience, “venture capitalists often do much more than monitor or advise; they may even play a hands-on role in the running of the young company”. VCs investing in DBFs are often endowed with plentiful contacts, idiosyncratic knowledge of specific sub-sectors relating to product development, commercialisation, negotiation, recruitment and training of managers and sales forces), and the capability to validate risky projects by simply investing in them.

Thus, while bio-clusters grow by attracting R&D budgets, technical and managerial skills and VC, co-location facilitates the transfer of uncodified knowledge and *know-how* (Florida and Smith 1990) via “open conduits” (Owen-Smith and Powell 2004). Such conduits consist of professional networks, face-to-face relationships, various types of academic collaborations, and public-private partnerships (Powell et al 2002; Cooke 2007; and Rosiello 2008).

This picture, however, leaves some questions unanswered. Many authors agree that VC can stimulate innovation and co-location presents advantages in terms of interactivity and knowledge transfer. However, works such as Florida and Smith (1990) and Avnimelech and Teubal (2006) warn that the existence of a VC market/industry at the heart of a high tech cluster cannot be taken for granted. A similar assumption seems especially hazardous for VC policy (Avnimelech et al 2008), as it may inspire strategies that aim at inducing demand via direct injection of risk capital and/or institutional change (see Gilson 2003; Da Rin et al 2006).

From a different angle, Florida and Smith (1990) and Mason and Harrison (2003) suggest that VC flows are to some extent responsive to the presence of “investor-ready” opportunities. Thus, the challenge faced by emerging clusters is that early-stage investors struggle to find an adequate population of companies capable of generating the sort of returns they seek. Notwithstanding the importance of institutional change, the main problem often resides on the lack of technical, entrepreneurial and managerial competence (Gompers et al 2006; Rosiello 2008).

In this sense, putting events in the right perspective may require focusing on the co-evolution (rather than the separate evolution) of science, technology, VC, and a range of complementary capabilities which are crucial for cluster emergence. For instance, in the context of ICT Avnimelech and Teubal (2006) introduce the concept of an *extended life cycle*. Here the emphasis is on institutional change as well as the creation and accumulation of business development capacity, a process that represents a necessary *pre-condition* for emergence. The normative implication is that VC can support and accelerate emergence if only if the appropriate set of *pre-conditions* is already in place.

Most research in this area has been conducted in the US and some of it relates to other industries, especially ICT. As technology, sector and context-specific factors can play a crucial role in shaping cluster emergence (Bresnahan and Gambardella 2004; Cooke 2007; Avnimelech et al 2008), we investigate whether similar dynamics of emergence apply to the UK bio-healthcare sector.

5. Methodology

This work employs a mix of qualitative and quantitative data. Our interview-based study (whose goals exceeded the scope of this paper) initially aimed to find out whether and how VCs deal with ex-ante and ex-post information asymmetries. Second, it examined whether the importance of VC is not only tied to the contractual relationship with DBFs, but also to the provision of added-value. Finally, it looked at Scotland and Cambridge, considering the question whether the characteristics of the local clusters, including their stage of development, have any effect on the frequency of knowledge transfer, ways of interacting, and the extent to which VC networks are regionally bounded.

Key actors in Scotland and Cambridge were interviewed, including CEOs and Business Development Managers of nine companies directly involved in the discovery and development of new solutions for patient healthcare, of which five had R&D facilities in Scotland and five in Cambridge. All companies were founded between 1994 and 2002, and had at least two rounds of VC investment and five of them had already products in the market or at an advanced stage in clinical trials. The sample also included nine actors with a direct knowledge of private equity investment in bio-healthcare. They all have offices in either Scotland or Cambridge. Finally, one interviewee worked with the East of England Development Agency, one with Scottish Enterprise and one with a regional bio-network in Cambridge.

Alongside qualitative information, we created a quantitative database detailing (i) the VCs and DBFs’ name, address, location, age (for the DBFs), type of investors (while our focus remains on “classic” VC, we distinguish between “institutional” and “non-institutional” VCs – family-friends, BAs and public schemes) and (ii) the investment, round type (private equity, exit or M&A) and amount. The data set starts with 1996 and covers the period until September 2006; it includes 655 deals within

the pharmaceutical and biotechnology sectors. The investment data was sourced from Library House in Cambridge which provided the list of firms with head offices in the UK that received equity finance¹.

We use these data to measure the concentration of VCs' offices and VC investment (number of deals and amounts invested) in the 12 UK Government Office Regions (GORs). Using postal codes, we classify VC investments as "local" if the VCs and the investee company are located within the same GOR; "adjacent" if they take place within a region that shares a border with the local "region", and "non-local" in all of the other cases. As far as deal involving investment syndicates are concerned, we define them as "local" when at least one of the partners was located in the same GOR as the investee company and "adjacent" when in a GOR sharing borders with that of the investee. The quantitative sample is combined with data concerning the distribution of Gross Added value (GVA) among GORs to assess the distribution of VC weighted for GVA and with data provided by the European Venture Capital Association (EVCA, 2005) to assess the magnitude of VC investment in the UK bio-healthcare sector compared to other EU countries.

The majority of the investments (55% of institutional deals, rising to 65% of deals involving a BVCA member) are made by syndicates of investors. Thus, in order to reduce the margin of error, we assess the co-location of VCs and investees by considering VCs-DBFs dyads in which the VC's location coincide with that of the first-named investor in the database (or its local office when the VC firms has got one). First-named investors are assumed to be the syndicate leaders and we compare the results of this test with those obtained without restrictions in the number of partners. Obtaining similar results would be interpreted as an indication that the leaders of the syndicate are more likely to be located in proximity to their investments as they are normally in charge of dealing with transactional problems and/or added-value provision.

In order to process the information gathered during the interviews we used NVivo software and the grounded theory method (Strauss and Corbin 1990). Various coding techniques have been employed to (i) label conceptual categories and unveil logical connections; (ii) identify, categorise and describe phenomena found in the text; and (iii) distinguish between core and non-core categories and phenomena, which helped to synthesise ideas and identify possible answers to the research questions.

6. Findings

Within the context of the UK, Scotland and Cambridge have bio-clusters characterised by different profiles of emergence. Both Scotland and Cambridge are bioscience and biotechnology intensive areas. However, Cambridge seems already to have achieved a critical mass of skills, capital and industrial activities and its emergence appears to have been spontaneous, in that public bodies have not been in the driving seat (aside from investments in basic research).

Around two hundred DBFs and three hundred and fifty providers of specialist services within the domain of the life sciences are situated in Cambridge. In addition, there are more than thirty research institutes and universities, twenty multinationals in pharmaceutical, agro-bio and food, and four medical hospitals involved in biotech research. The University of Cambridge plays a vital role, as highlighted by the numerous collaborations that involve its departments and the high number of spinouts it generates. According to Garnsey and Heffernan (2005), twelve departments had

been the source of forty-two spinouts. Outside London, Cambridge has the highest concentration of VC-backed companies: biotechnology, med-care and pharmaceuticals attract the majority of this investment, accounting for 42% of all deals in 2004-06 (Library House 2006).

Scotland is yet to experience full emergence and public bodies play an important role in driving the process forward. Following the process of political devolution in the late 90s, Scottish Enterprise has been invested with the challenge of designing and implementing a policy framework to support the development of the Scottish biotechnology industry, predominantly clustered around the cities of Glasgow, Edinburgh and Dundee. Some targets were set to be met by 2003, including 100 DBFs, 250 support and supply organisations, 24,000 jobs, and the creation of strategic linkages and networks within and beyond the boundaries of the local communities.

By the end of that period, the Scottish biotechnology sector employed roughly 26,000 people. However, the majority of Scottish DBFs were small in size and a significant number of those involved in drug discovery struggled in the early phases of discovery and pre-clinical trials (Rosiello 2007). More recently, however, the scope and number of public initiatives has been expanded (Rosiello 2008), three DBFs with HQ in Scotland went public in London and one in New York, and Wyeth (a North-American PC) got directly involved in the Scottish *Translational Medicine Research Collaboration* (www.tmr.co.uk).

To date, Cambridge remains the prominent UK bio-cluster and a magnet for public research funding, skills and VC (Casper and Karamanos 2003; Library House 2006). Being closer to the City of London where most VCs have offices facilitates networking and personal interaction, whereas Scottish investees tend to rely on a mix of local angel groups, public finance and external providers of funding.

6.1. The concentration of VC investment in specific regions and co-location of VCs and investee companies

The pharmaceutical and biotechnology sectors constitute a significant component of the UK economy, employing around 73,000 people in 2005, over a third in R&D and 22,400 in core biotechnology. In 2005, the UK's biotechnology sector was the European largest and most robust, with around 450 DBFs, generating over €5billion in revenues and awaiting 224 new drugs in clinical trials – around 40% of the EU total. In 2006, 7 out of 32 IPOs and 8 of the top 10 mergers and acquisitions (M&A) deals involved UK based DBFs (E&Y 2007). According to EVCA (2005) data, the UK attracts a higher proportion of VC investment than any other EU country.

[Insert table one about here]

Table 2 provides a summary of the investment activity in the UK for biopharmaceutical firms for the period 2000-Sept 2006, during this period a total of 592 investments were made with a recorded deal value of £1,713m. The table shows the investment activity broken down according to institutional investment, non-institutional investment, and investment in the form of Government investment, grants and investments from research charities. By far the most influential category is the institutional VC accounting for 71% of deals and 91% of the value of investment recorded. Therefore, we concentrate our analysis in the remainder of this paper onto the activities related to institutional deals. The East of England (an area containing Cambridgeshire) takes the largest shares of activity across all three categories of

investment. The other main investment regions of the UK are the South East of England (an area containing Oxfordshire), the London area and Scotland. These four regions are most active in terms of both deals count and total investment.

[Insert table two about here]

The results from Table 3 confirm that VCs' money in the bio-healthcare sector tends to flow into the Eastern region, the South East and Scotland. This becomes even more salient when we weigh investment by regional GVA. The East of England, South East and Scotland have the three higher ratios of the 12 UK regions, which reflect the distribution of biotech-related activities across the country.

[Insert table three about here]

Having established that VC investment in bio-healthcare is unevenly distributed both across Europe and the UK; the next step is to find out whether co-location plays any role in shaping this distribution. The UK VC industry tends to be located in the City of London and around 70% of VC investments in the bio-healthcare sector are syndicated among a variable number of partners. Firstly we concentrate on a core group of UK investors who are members of the British VC Association (BVCA). This association represents the interests of VCs making investments in the UK and therefore we can expect this group to represent the core expertise in VC deal making in the UK. Table 4 shows the number of deals in our dataset involving at least one registered BVCA member, and the location of the nearest office of the BVCA syndicate member in each particular deal. We also include the regional presence according to office locations of BVCA members active in our database.

[Insert table four about here]

We find that for deals made in any UK region where there is at least one BVCA member in the syndicate (265 deals), then it is very likely that at least one BVCA member will be found within the same or an adjacent region to the firm receiving funding. Our analysis finds this to be the case in 90% of deals involving a BVCA member; in over 64% of these deals a BVCA member is locally based. When we look at the "first-named" investors (assuming that they are the syndicate's leaders), we find that in 86% of cases when a BVCA member is the first named the investor they also have an office location classified as in a region either local or adjacent to the firm. This result strengthens our observations that investors who are located near their investment play an active role.

Table 4 also shows large variation in the dyadic relationships of these deals across regions. The proportion of investments involving a local BVCA member ranges from 30% to 100%, and ranges between 55% and 100% for investors based within regions adjacent to the deal. The final column shows the regional coverage of BVCA members in terms of office locations. The association of VC's with London is clearly shown by the 154 investors (from a total of 195 investors active in this population of firms) having an office presence in Greater London. Similarly, all deals made in London involve a VC with a London office.

We also find the East and South Eastern regions have a relatively low proportion of investors based locally, but a high level of investors from the surrounding regions. This is explained by the proximity of the South East and Eastern regions to London.

In contrast Scotland (3i have an office based in Scotland, which invests in oil, gas and power generation and is not included in this analysis) has the lowest proportion of BVCA investors with proximate office presence. Scotland attracts little investment from BVCA members based in Northern regions of England, although we also find that a significant amount of Scottish institutional deals involve London based investors. Such evidence evokes Sorenson and Stuart (2001, 1582) argument that the co-location of at least one syndication partner allows VCs “to rely on the evaluation of another investor closer to the target in industrial or physical space”. However, this type of proximity relates to connections with VCs based in a financial centre; hence it is not necessarily comparable to the one seen in US technology clusters. In this respect, in section 6.3 we discuss the role of specialist VC.

Overall these figures show that VC investment in UK bio-healthcare is concentrated in specific regions and the majority of deals involve geographical proximity, that is, the investment is classified as either local or adjacent to a VC’s office. The ‘Golden Triangle’ corresponds to 49% of deals made and 60% of the total value of investments made in the UK (see Table 5). Also, 58% of institutional deals in this area involve at least one local VC investor, and virtually all deals in the area have an investor with an office in the ‘Golden Triangle’. If we include all investors with traceable locations we find that around 52% of investments in the ‘Golden Triangle’ (institutional and non-institutional) have a local VC investor, whilst a further 10% access funds from other types of local sources. Similarly, in over 40% of these deals the first named syndicate investor is based in the same region as the firm.

[Insert table five about here]

Table 6 provides an indication of the depth of the availability of experienced investors to guide the firms. We examine the number of proximate investors involved in these deals. We have focused on demonstrating that the first named investor is frequently local to the firm, as well as showing that a high proportion of investments have at least one office in a nearby location. However, we can also expect that there maybe further benefits to a firm if there are more than one locally based investor operating in the syndicate, as different investors can provide a range of backgrounds and contacts to support their firms. The table below shows the average number of investors in local or adjacent regions per deal, and indicate strength in numbers for different UK regions. As with the previous discussion this table shows the large differences in the presence of co-location of VC’s across UK regions. For example, institutional deals in the ‘Golden Triangle’ have on average nearly two investors based within the regions surrounding the deal, compared to other Northern UK regions that have on average less than one investor nearby.

These findings may be because investors need to collect information and monitor companies in order to deal with transactional problems, and/or because of the advantages that proximity guarantees as regards the provision of added-value. The figures concerning the co-location of investee companies and “first-named” investors suggest that co-location may be necessary to embed within local networks and collect valuable knowledge and information as well as to develop a direct relationship with investees. These figures, however, do not allow us to estimate the influence of either factor.

[Insert table six about here]

6.2. Overcoming risk and transaction costs: the advantages of proximity

The bio-healthcare sector currently represents one of the main targets for VC investment in the US and Europe. However, it remains a highly risky business due to high attrition rates, high capital requirements, long times of realisation and high uncertainty. A primary requirement for investors is to identify and understand such risk. Most VCs have personnel with scientific, technical and business experience in the area of technological application they invest in. On the one hand, a scientific background is necessary to assess the feasibility of the R&D programme and the likelihood that the programme will succeed, which may lead to a profitable exit. On the other hand, VCs investing in DBFs must frequently deal with inexperienced managers, some of whom are research scientists spinning-out from research institutions. Hence, identifying and dealing with both information asymmetries and managerial gaps represents a key strategic priority.

Concerning the investment contract, our survey-data show that institutional VCs make more extensive use of contractual clauses to protect their investment. However smaller investors and BAs tend to rely more on a combination of personal experience and localised networks to scout for good opportunities and screen business plans. Through social networks they recruit, consult and connect portfolio firms with competent people, such as scientists with experience in applied research, experienced managers, and a variety of intermediaries. Personal experience and networks are also essential to validate the biotechnology and the potential to develop a sustainable and remunerative business.

“It’s a mixture of technology and execution risk. Attrition risks in running the programs, the fact that the drug the programs can usually kind of fall over; managerial risk, that is, inexperienced management teams choosing inappropriate strategies.” (VC_Scotland_3)

“In terms of mitigating the risk when selecting the investments it is really about asking: ‘Do I understand this?’, both from a medical-disease point of view and from a business model point of view. For those who have that expertise in-house and there are some, then they do that internally. For those who do not, they will have a network of people they can call and have a look at it.” (Other_Scotland_1)

Through the due diligence process VCs must be able to estimate and manage the risk associated with a specific investment. Such knowledge is then accumulated, recycled, and exchanged with other investors to assess new opportunities and business plans. In this sense, our survey-data shows that VCs benefit from cumulative learning, with emphasis on relating personal experience and investment performance, it constitutes an essential way to improve the criteria and metrics employed to assess the feasibility of upcoming plans. In this learning process networks play an essential role in the process of diffusion and use of critical information. When reliable metrics are not available, using expert consultants represents a second-best solution, which underlies the importance of professional ties to intermediaries that investors trust and can be employed on a regular basis.

“Biotech companies tend not to have any revenues. It means we can’t use standard metrics for evaluating companies. You’ve got to look at value in the companies in different ways: usually benchmarking other exits that have taken place...looking at other IPOs of companies that are very similar or looking at trade sales of companies that have been bought by other partners.” (VC_Cambridge_1)

“In due diligence, we use good consultants or put in place non-executive directors who are experienced in a specific area. That helps us to get more comfortable with what the company is doing and appreciate how much risk is there in the programs.” (VC_Scotland_3)

Early stage investments are considered riskier as they present higher failure rates and longer times of realisation. When the founders are inexperienced, VC's may substitute inventors and/or bioscientists for experienced managers able to move ideas from the research lab into a profit-oriented business. Other than managers, investors may bring in experienced non-executive directors to help remodel the company's strategy and represent the VC on the DBF board. In subsequent stages, it becomes a question of building credibility by collaborating with PCs and other DBFs, entering clinical trials and establishing a variety of trading relationships that are indispensable to commercialise upcoming products and services.

"We do not only focus on costs and potential revenues; it is also about how we can develop and use some of the strength of the business to build a strategic plan. Even before the investment we make links between the potential investee and other investors, non-execs and prospective business partners" (VC_Scotland_1)

"In the smaller companies where the teams are less experienced then obviously you have to do a bit more so that often can be things like helping them with financial analysis, looking at other exits, and discussing with them about potential partners, just generally getting more involved in the business and in trying to assist them in whatever they need." (VC_Scotland_3)

Thus, one of the reasons why investment syndicates tend to include at least a local player is to assess, monitor and support the investee company. In particular, when we split the DBFs in our sample into different age groups, we notice that 70% of deals involving companies that at the time of completion were less than ten years old are characterised by co-location (see Table 7). Such a result is confirmed across the first three age groupings. Proximity of at least one VC is also maintained in terms of deal sequence, suggesting that benefits to being near the firm remain important throughout the different stages of investment. Concerning non-institutional deals, 80% of those with information on the syndicate involved co-located dyads.

On the contrary, the percentage of deals characterised by co-located dyads of investees and investors drops to 30% for companies that are more than 10 years old. In this older age group of firms the 70% deals without a proximate VC office, are classed as the initial rounds of institutional finance received by each firm. Although we note a small number of deals in this age group, the combination of firm age and round sequence suggests that these are established firms which have grown without 'classic' VC support and are subsequently looking to expand or restructure and therefore have less need for locally based monitoring or assistance.

[Insert table seven about here]

In synthesis, our data-survey shows that VCs investing in DBFs manage high risk and transactional problems via a mix of contractual safeguards, direct monitoring, and access to local networks to gather information and set up professional ties. Consistent with Powell et al (2002) and Madill et al (2005), we find that bigger VCs that employ specialised personnel operate and have offices in more than a single location, build wider networks and syndicate investments over long distances. On the contrary, non-institutional and younger investors depend on localised networks and cumulative learning. Local ties and professional networks are also built to add-value to investees. This phenomenon is more intense when the management team lacks experience (University spinouts), and non-institutional investors and specialist VCs (see 6.3) are involved. Older and more established companies rely less on local networks.

6.3. On contest-dependency and the role of specialised investors

Section 6.1 shows that both Cambridge and Scotland have higher than average investment per GVA ratios. While Cambridge is an emerged bio-cluster, in Scotland this can be partly explained by the convergence of Scottish Enterprise co-investment scheme towards biotechnology, the role played by BAs (Mason and Harrison 2003) and the presence of large VCs such as *Scottish Equity Partners* (SEP III was largest newly formed fund in Europe in 2006).

Both locations have important forms of expertise and research excellence in the life sciences and had been previously interested by the emergence of ICT clusters. However, the competitive advantage of *Silicon Glen* was in low cost manufacturing, with a predominance of foreign-owned businesses. This limited R&D investment and local involvement in technology transfer results in few strong and extensive science-technology-market networks. Around Cambridge, instead, a large number of small firms have been able to draw upon university research to penetrate emerging markets. Cambridge developed experience and a positive reputation in linking industry and academia as well as a range of competent intermediaries.

“Cambridge is something with universal reputation in terms of biotech and pharma; principally because of the proximity to excellent research, the South East led itself to biotech companies being set up, being established, being replicated and being close. They can attract investors and location is important. Investors are in London, so the closer you are to London, the easier it is going be to attend meetings, have networks, come up or go there to see them.” (DBF_Cambridge_1)

Differences between clusters are strongly related to the availability of managerial skills. In Cambridge, the existence of a high-tech cluster, proximity to the labs of PCs and the high rate of creation on new DBFs has contributed to the increase in number of scientists with industrial experience and the presence of experience executives. Alongside experience consultants, a local pool of managers has effectively contributed to help remedy key competence-gaps in DBFs. As a result, VC investment was able to generate entrepreneurial successes, with pervasive effects (Zook 2002) on DBFs locate elsewhere. In other regions, the paucity of experienced intermediaries and managers constrained VC development and the process of recycling of capitals and knowledges. In the absence of such a virtuous cycle, access to VC constitutes a necessary but not sufficient condition to grow successful ventures.

“Management is probably a bigger limitation in Scotland than money. You cannot at the moment, and probably would ever again be able to, build sustainable fundable companies based on research assets alone.” (DBF_Scotland_1)

“If you want to set up a business just now, go to the North East, because £40-50 million soft venture capital money is looking for that. The reason they can't find to do it is not the technology, is the lack of CEOs, the lack of business people.” (Other_Cambridge_1)

As we saw earlier, at least one of the partners of the investment syndicate tends to be local, which suggests that proximity to investees is a determinant of investment decisions. Because of the number of opportunities in the same location, London-based investors network and invest prevalently in Cambridge, which means avoiding the difficulties associated with monitoring managers when the company is located elsewhere. In a similar way, value adding activities also require geographical proximity in that both the availability of complementary assets and the development of local networks depend on state of development of the local cluster.

“Most of venture capital investments are made in syndicates of several investors. One of them has to be local, because if no one is local, no one can really keep an eye on what is happening in the company.” (DBF_Scotland_3)

“I invest in Cambridge because I can see and help them easily; there are people around the cluster that I can bring in. Investing in Scotland would be harder. If you are an investor and something is long away, you feel less comfortable about it because it is harder to detect problems, influence, impact, and help, harder to bring the rest of your network, which is why clusters work.” (BA_Cambridge_1)

Works such as Sorenson and Stuart (2001) emphasise the role of industrial specialists; both the accumulation of investment experience and the possibility to interact with specialised and trusted co-investors can contribute to expand the geographical scope of investing activities. Hence, in our dataset we code whether investors in bio-healthcare are specialist or generalist investors. A specialist is defined as an investor with 60% or more of their total portfolio concentrated in one type of investment (biopharma, IT, communications, healthcare, media and the financial sector). Table 10 summarises the results of the analysis of specialist investors according to region and their proximity to the deal. Overall we find that a small percentage of deals (15%) involve a specialist that is local to the firm. However, if a specialist investor is present in a deal, 73% will be based nearby and 44% local.

Specialists are concentrated in two locations: the East (Cambridge) and London. The implication is that DBFs in London, East and South East have good access to finance and value added from specialist investors. However, in some cases specialists are also prepared to invest over distance. In Scotland, 17 deals involved a specialist, but only in one deal were these specialists local. Generally, we find regions outside the “Golden-Triangle” have a much lower proportion of deals involving specialist VC. In non-Triangle regions access to finance from a specialist is likely to come from an investor located away from the firm.

[Insert table eight about here]

We also ask whether the presence of a specialist has an implication for the proximity of other generalist investors. For example we know that in the East and London specialists do the bulk of their investing locally. In Scotland, the few specialists active in the region were not local. Table 8 shows that for Scottish investments involving a specialist, only 5 deals, or 30% involved a proximate investor. The proportion of deals involving a specialist and any proximate investor is lower than the overall investor proximity recorded for Scotland in Table 4. In fact we observe for many of the Northern UK regions that the presence of specialist investors in a syndicate reduces the chance of any investor proximity, albeit this result may be affected by the significant proportion of non-institutional investments that are not recorded in official statisticsⁱⁱ (Mason 2005).

Overall, we observe strong regional concentration of specialist investors in the South. We also find heterogeneity with regards to the influence of specialist investors on the proximity of investors. For some regions such as East (Cambridge), finding a specialist investor in the syndicate means there is around a 56% chance that they will be local to the deal. For other regions (especially Scotland) the presence of a specialist is likely to decrease the likelihood that the specialist (and/or its co-investors) will be local. Therefore, while being connected to wider networks, even specialist VCs have a strong focus on emerged clusters such as Cambridge. As a result, DBFs located within the “Golden Triangle” are probably in the best position to exploit the value adding services that competent VC can provide.

7. Discussion and conclusions

Our qualitative and quantitative data show that the propensity of ‘classic’ VC to invest in UK DBFs is contingent on various factors, including the size of the final market, the quality of the bioscience, the characteristics of the regulatory regime, and the degree of readiness of investee firms. Using their networks and connections, VCs help investees to remedy competence and financial gaps and link with commercial partners, other intermediaries, and new investors. Further, VCs can provide direct support by advising and shaping business strategy. In this respect, variations depend on the characteristics of the investors and the experience of the managers involved.

We found evidence of co-location between investee companies and leading investors, with a marked inclination to target DBFs located in bioscience intensive regions. As most investments in bio-healthcare are completed by large syndicates, this result becomes more evident when we consider that at least one investor is located in the same region or in the adjacent region of the investee company. Our motivation to take into account VCs in adjacent regions is that many VCs have offices in the City of London and seek opportunities in other regions, such as the Eastern region, the South East and, to a lesser extent, Scotland. Thus, this method permits identifying which regions are the main recipients of the risk capital accumulated in the City of London.

We envisage various interpretations of the propensity to invest in the “Golden-Triangle” and, particularly, in the Cambridge area. Initially, this may be due to a historical accident: being located a short distance from the City of London helped VCs to scout for and perform due-diligence on potential opportunities. Co-location was accidental but the proximity of good bioscience and money was crucial to the emergence of Cambridge. In this sense, our findings evoke a static interpretation of the advantages of co-location. VCs make use of networks to spot, gather information about, monitor and mentor investee companies. Networks tend to be local simply because most investors, intermediaries and experienced managers happen to be located in the proximity (London) of centres of bio-scientific excellence (Cambridge).

The concentration of these actors allowed for frequent interaction and has had a pervasive effect on external DBFs and VCs. The accidental proximity between London and Cambridge facilitated the absorption of London-based VCs into geographically bounded networks. After that, London-based VCs may have become to a degree reluctant to invest in other locations not so much because of the quality of the local science but because of the transaction costs, information asymmetries, and impracticalities of adding-value over long-distances.

Following this line of thinking, our static interpretation can be reconciled with works such as Audretsch and Stephan (1996), who show that the propensity of key actors (scientific advisors) to interact either locally or at distance depends on the stage of development of the local cluster, and Powell et al (2002), Niosi and Banik (2005) and Porter et al (2005), who explain that the function of VCs within the local system varies across time. Such reconciliation suggests a dynamic interpretation of our findings as regards the emergence of high tech clusters, a process that involves an increase in the number of ‘investor-ready’ opportunities, intensification of VC deals, and accumulation of know-how and network contacts.

According to Mason and Harrison (2003), an ‘investor ready’ project is characterised by complete information, realistic expectations and a detailed account of how new products and services will be brought to market. Providing such account

requires the ability to articulate a vision as to how financial resources will be used to achieve such goals. To achieve these goals in the bio-healthcare sector involves managing external factors such as regulation or the performance of partners involved in collaboration agreements as much as the ability to manage R&D operations, protect IP, and find routes to market.

Thus, while Cambridge hosts the highest proportion of 'investor-ready' DBFs, VCs would also consider investing more frequently elsewhere but other locations present a paucity of real opportunities, not so much because of the quality of the science, but because of the relative scarcity of complementary capabilities - such as managerial skills. In comparison with Scotland, from the outset Cambridge presented not only a very strong bioscience base, but also an established high tech cluster, proximity to labs of PCs, and experienced technology consultants. Extended networks involving specialists VCs came later, whilst the achievement of successful exists by some local DBFs facilitated the accumulation and recycle of capitals and capabilities. In Scotland, similar processes are beginning to materialize in distinct geographical locations, such as Dundee, Glasgow and Edinburgh. Overall, however, Scotland is yet to generate the type of incremental dynamics that can help build critical mass (Rosiello 2006).

Our interview data also suggest that bio-cluster emergence coincides with processes of cumulative and collective learning: formal and informal networks and knowledge flows, collective adaptation to changing conditions, forms of coordinated behaviour to deal with transactional problems (dilution and internal conflicts), technical challenges (moving compounds through R&D stages) and managerial risks (high attrition rates and regulatory uncertainty). All of these mechanisms allow learning through direct interaction and apprenticeship.

Cumulative learning is characterised by knowledge specialisation. VCs need to develop an in-depth understanding of the risk associated with the DBFs they invest in. BAs are often ex-entrepreneurs and highly networked individuals who have accumulated personal experience and contacts. In some cases they have finances to re-invest in viable opportunities. Institutional VCs are either entirely focused or employ individuals distinctively dedicated to specific types of investments, people endowed with the scientific and business background necessary to understand and assess the risk associated to R&D programmes and business plans. As noted earlier, however, they also extensively rely on their network of contacts. Personal experience and networks allow VCs to develop effective routines to evaluate and manage risk in areas such as drug discovery and development.

In summary, in the 1996-2006 period London-based VCs showed a clear propensity to invest in the most promising regions. Proximity plays a significant role in the transfer and recycle of vital information and know-how (Florida and Smith 1990), a process which in some cases entails the provision of non-financial added-value. Crucially, both Cambridge and, to a lesser extent, Scotland present a certain degree of "pervasiveness" (Zook 2002), a trend already observed by other works, such as Casper and Karamanos (2003) and Niosi and Banik (2005). We doubt whether UK VCs investing in bio-healthcare play the same catalytic role observed by Florida and Kenney (1988), Sorenson and Stuart (2001) and Avnimelech and Teubal (2006) in relation to US and Israeli high tech clusters.

On the one hand, the interview data confirm a general trend of UK VCs to focus on largest late stage deals and search quick exits. This partly explains the fact that

various DBFs in our sample were considering the option to move some operations to North-Americaⁱⁱⁱ. Such trend emerges even in relation to Cambridge and can be explained by the need to move closer to a bigger market or a pool of managerial talent or a more sophisticated shareholders base (Cooke 2007). On the top of these factors, some interviewees stressed lower availability of risk capital and the higher risk aversion of London-based VCs. The greater availability of risk capital (and debt provision) in the USA is proved by a variety of sources. According to Critical (2006), between 2001 and 2004 the equity gap was especially evident at seed-stage (US firms got around \$15billion against Europe's \$10 billion) and for companies more than 12 years old (\$30 billion against \$20 billion).

"If you want to be successful, you have to have a successful drug in the US and you need to access a large amount of capital, which is in the US. From a capital market point of view, US biotech companies can raise 10 times the amount of money than anyone in the UK can raise." (DBF_Scotland_4)

On the other hand, we observe that the existence and presence of specialist VCs reflects localised learning processes and allows emerged clusters - such as Cambridge - to latch into global networks. Specialists located in the London area make sporadic investments outside the 'Golden Triangle'. However, these deals do not necessarily involve any local investors. This result may be due to the paucity of available information about the activities carried out especially by informal investors (Mason 2005) or the lack on trusted partners in some of these locations. While our interview data provide some degree of support especially to the former hypothesis, our quantitative results confirm the intuition that in the UK bio-healthcare sector competent VC tends to follow rather than anticipate cluster emergence.

These considerations have a series of normative implications for regional innovation policy. VC constitutes a key component of regional innovation systems that can play a catalytic role. While co-location offers a number of static externalities, our study is more in line with demand-side arguments stressing the attractive power of 'investor-ready' opportunities (Mason and Harrison 2003) than supply-side approaches that consider VC presence at the core of high-tech clusters as a given. On account of the high proportion of deals taking place within the 'Golden Triangle', the chances other clusters have to attract significant inflows of VC seems partly depend on their ability to create a population of investable DBFs.

In turn, generating such a population requires acting on a number of *pre-conditions* (Avnimelech and Teubal 2006), including investments in the local science-base and infrastructure of innovation (Powell et al 2002) in order to allow for cross-pollination of knowledges, experimentation of business approaches and development of critical skills (Orsenigo 2006; Cooke 2007). Therefore, we are sceptical about the policy conclusions reached by influential works such as Gilson (2003), OECD (2003), and Da Rin et al (2006). These suggest that capital injections and/or institutional changes can be sufficient for the emergence of VC markets and/or industries. In accordance with Avnimelech et al (2008), we propose rather that VC policy should be consistent with the wider strategic priorities of innovation and technology policy; priorities that should anticipate rather than follow VC policy implementation.

References

- Audretsch D. B. and P. E. Stephan, 1996, 'Company-Scientist Locational Links: The Case of Biotechnology', *American Economic Review*, 86, no.3:641-652.
- Avnimelech G. and M. Teubal, 2006, 'Creating VC industries which co-evolve with High Tech: Insights from an Extended Industry Life Cycle (ILC) perspective to the Israeli Experience', *Research Policy*, 15, no. 4-5: 289-299
- Avnimelech G., Rosiello A and M. Teubal, 2008, 'A Discussion on the Theoretical Foundations of VC Policy: Moving from a Financial Perspective towards a Systemic and Evolutionary Framework', ESRC Innogen Centre Working Paper, available at: www.innogen.ac.uk.
- Bresnahan, T, A. Gambardella; and A. Saxenian, 2001, 'Old Economy inputs for New Economy outputs: Cluster Formation in the New Silicon Valleys', *Industrial Corporate Change* 10, no. 4: 835-860.
- Burns L. R., 2005, *The Business of Healthcare Innovation*, Cambridge: Cambridge University Press.
- Da Rin M., G. Nicodano, A. Sembenelli, 2006, 'Public policy and the creation of active venture capital markets', *Journal of Public Economics*, 90 (8 - 9): 1699 - 1723
- British Venture Capital Association, 2006, *Report on Investment Activity*.
- Casper S. and Karamanos A., 2003, 'Commercialising Science in Europe: the Cambridge Biotechnology Cluster', *European Planning Studies*, 11 no. 7: 806-823.
- Cooke, P. (2004) 'Editorial: The Accelerating Evolution of Biotechnology Clusters' *European Planning Studies*, 12, no.7, pp.915-920.
- Cooke P (2007), *Growth Cultures: The global bioeconomy and its bioregions*, London and N. Y.: Routledge.
- Critical I, 2006, 'Comparative Statistics for the UK, European and US Biotechnology Sectors - Analysis Years 2003 & 2004', www.dti.gov.uk
- Ernst & Young, 2007, *Beyond Borders: Ernst & Young's Global Biotechnology Report 2007*, London: Ernst & Young LLP.
- Ernst & Young, 2008, *Beyond Borders: Ernst & Young's Global Biotechnology Report 2008*, London: Ernst & Young LLP.
- European Private Equity and Venture Capital Association, 2005, *EVCA Yearbook, Annual Survey of Pan-European Private Equity & Venture Capital Activity*, EVCA.
- Florida R. and M. Kenney, 1988, 'Venture Capital, High Technology and Regional Development', *Regional Studies*, 22, no.1: 33-48
- Florida R. and D. F. Smith, 1990, 'Venture Capital, Innovation, and Economic Development', *Economic Development Quarterly*, 4, no.4: 345-360
- Garnsey, E. and Heffernan, P. (2005) 'Clustering as Multi-levelled Activity: the Cambridge Case' *Paper for Plenary Session III, 4th European Meeting on Applied Evolutionary Economics*.
- Gilson, R., 2003, 'Engineering a Venture Capital Market: Lessons from the American Experience', *Stanford Law Review* 55 (4), 1067-1104.
- Gompers P., J. Lerner, 2001, 'The Venture Capital Revolution', *Journal of Economic Perspectives*, 15, No. 2:145-168.

- Granovetter MS, 1973, 'The Strength of Weak Ties', *American Journal of Sociology*, 78, no. 6: 1362.
- Haussler C and Zademach HM, 2006, 'Cluster Performance Reconsidered: Structure, Linkages and Paths in the German Biotechnology Industry, 1996-2003', GESY Discussion Paper No. 188.
- Hellmann T, Puri M, 2002, 'Venture capital and the professionalization of start-up firms: empirical evidence', *Journal of Finance*, 57: 169–197.
- Hsu D H., 2004, 'What Do Entrepreneurs Pay for Venture Capital Affiliation?', *Journal of Finance*, 59, no.4:1805-1844.
- Kruger K, 2005, 'The medical device sectors, in Burns', L R (Ed) (2005), *The Business of Healthcare Innovation*, Cambridge: Cambridge University Press
- Library House (2006), 'The SuperCluster Question: The Cambridge Cluster Report' 2006.
- Madill J J, Haines G H. Jr, Riding A L, 2005, 'The Role of Angels in Technology SMEs: A Link to Venture Capital', *Venture Capital*, 7, no.2: 107 - 129
- Martin R, C. Berndt, B. Klagge, P. Sunley, 2005, 'Spatial proximity effects and regional equity gaps in the venture capital market: evidence from Germany and the United Kingdom', *Environment and Planning A*, 37, no.7: 1207 – 1231
- Mason C M and R. T. Harrison, 2002, 'The geography of venture capital investments in the UK', *Transactions of the Institute of British Geographers*, 27: 427-451.
- Mason C M and R. T. Harrison, 2003, 'Closing the Regional Equity Gap? A Critique of the Department of Trade and Industry's Regional Venture Capital Funds Initiative', *Regional Studies*, 37, no.8: 855-868
- Mason C. M., 2005, 'Informal Source of Venture Capital' in Simon Parker (Ed.) *The Life Cycle of Entrepreneurial Ventures: Volume 3*, International Handbook on Entrepreneurship, Kluwer, 2006.
- Massey D., P. Quintas, D. Wield, 1992, *High-Tech Fantasies: Science Parks in Society, Science and Space*, London and N.Y.: Routledge,
- McKelvey M. and L. Orsenigo, 2001, 'Pharmaceuticals as a Sectoral Innovation System', paper prepared for the ESSY Project (European Sectoral Systems of Innovation) and within the Epris Project.
- Niosi, J. and Banik, M. (2005) 'The Evolution and Performance of Biotechnology Regional Systems of Innovation' *Cambridge Journal of Economics*, 29, 343-357.
- Northrup J, 2005, 'The pharmaceutical sector', Burns R. L. (Ed), *The Business of Healthcare Innovation*, Cambridge: Cambridge University Press.
- OECD, 2003, Venture Capital Policy Reviews, Paris: STI Working Paper 2003.
- Owen Smith J, Powell W W., 2004, 'Knowledge Networks as Channels and Conduits: The Effects of Spillovers in the Boston Biotechnology Community', *Organization Science*, 15, no. 1: 5–21
- Orsenigo L, 2006, *Clusters and Clustering in Biotechnology: Stylised Facts, Issues and Theories. From Clusters to network structures and their dynamics*, in eds. P. Braunerhjelm and M. Feldman (eds.), "Cluster Genesis", Oxford, Oxford University Press.
- Pisano G. P., 2006, *The Science Business: The Promise, the Reality, and the Future of Biotech*, Boston, MA: Harvard Business School Press,

- Porter K Whittington K B Powell W W., 2005, 'The Institutional Embeddedness of High-Tech Regions: Relational Foundations of the Boston Biotechnology Community', in eds S Breschi and F Malerba, *Clusters, Networks, and Innovation*, Oxford University Press
- Powell W W., K. W. Koput, J.I. Bowie, L. Smith-Doerr, 2002, 'The Spatial Clustering of Science and Capital: Accounting for Biotech Firm-Venture Capital Relationships', *Regional Studies*, 36, no.3: 291 - 305.
- Rosiello, A. (2006) 'Comparing Biotechnology Innovation Systems: the Case of Scotland, Sweden and Denmark' ESRC Innogen Centre Working Paper 35, available at: www.innogen.ac.uk
- Rosiello A, 2008, 'Examining Scottish Enterprises framework for action in life sciences', *International Journal of Biotechnology*, 10, No.5 pp. 496 - 517
- Sorenson O. and T.E. Stuart, 2001, Syndication Networks and the Spatial Distribution of Venture Capital Investments, *AJS*, 106, no.6: 1546–88.
- Strauss, A. and Corbin, J., 1990, *Basics of qualitative research: grounded theory procedures and techniques*, Newbury Park, California: Sage Publications
- www.pwcmoneytree.com 'European Preliminary Investment & Fundraising Activity: 2005 Summary and Data', US National Aggregate Data.
- <http://www.burrillandco.com>
- Zook M. A., 2002, 'Grounded capital: venture financing and the geography of the Internet industry', 1994--2000, *Journal of Economic Geography*, 2, no. 2:151-177
- Zook M. A., 2004, 'The knowledge brokers: venture capitalists, tacit knowledge and regional development', *International Journal of Urban and Regional Research* 28, no.3: 621-641.

Appendix I: Qualitative Sample Description

DBFs in Scotland

Ardana plc www.ardana.co.uk	Founded in 2005, Ardana was a pharmaceutical company focused on specialist and secondary care markets (reproductive endocrinology, urology, obstetrics & gynaecology) to discover, develop and market new products.
Axis-Shield www.axis-shield.com	Axis-Shield develops in-vitro diagnostic tests for use in clinical laboratories and at the point of care. Created in 1999 via the merger of Axis Biochemicals and Shield Diagnostics, the group comprises Laboratory Division in Dundee and a Point-of-Care division in Oslo.
CXR Biosciences www.cxrbiosciences.com	CXR Biosciences was founded in 2002 to address the commercial application of in-vivo models and a range of specialised techniques and technologies that improve the selection of optimal leads through early predictions of the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicological) characteristics of compounds.
Cyclacel Pharmaceuticals, Inc. www.cyclacel.com	Founded in 1996, Cyclacel Pharmaceuticals Inc. is dedicated to the discovery, development and commercialisation of novel drugs to treat human cancers. Corporate HQs are in Berkeley Heights, New Jersey; primary research facilities in Dundee.
Stem Cell Sciences www.stemcellsciences.com	Founded in 2004, Stem Cell Sciences' core objective is to develop safe and effective stem cell-based therapies for incurable diseases. The Company has business/scientific operations in Edinburgh and Cambridge (UK), Melbourne (Australia) and Kobe (Japan).

DBFs in Cambridge

Astex www.astex-therapeutics.com	Founded in 1999, Astex Therapeutics uses high-throughput X-ray crystallography in a novel fragment-based approach to discover and develop small molecule drugs. Its primary focus is on oncology and has a broad pipeline of products in clinical and pre-clinical development.
Lumora Ltd www.lumora.co.uk	Founded in 2002, Lumora brings molecular diagnostics to market, not only for food-borne pathogens but also for GMO detection and the establishment of food provenance.
Senexis www.senexis.com	Senexis was formed in 2001 to build a pipeline of drug development programs for neurological (Alzheimer's disease) and systemic degenerative conditions. Optimised lead compounds have already shown pre-clinical efficacy.
Phico Therapeutics Ltd. www.phicotherapeutics.co.uk	Founded in 2000, it develops a platform technology with the potential of producing anti-bacterials active against all species of bacteria, including MRSA, and the Gram negative bacterium, Escherichia coli.

Venture Investors

Albany Ventures www.albanyventures.co.uk	Albany Ventures invest in technology companies based in the UK and Ireland, with a specific focus on enterprise software and healthcare. In November 2006 Albany Ventures was acquired by the Alliance Trust PLC. Albany Venture recently exited from Domantis, which was sold to GlaxoSmithKline for £230 million, and has in its portfolio Ardana, co-invested with 3i, Deutsche Venture Capital, MVM and TVM.
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Andy Richards (information source: www.biologyinbusiness.org)	A serial biotechnology entrepreneur and business angel, Andy Richards is currently director of Vectura plc, Geneservice, Biowisdom, Daniolabs, Theradeas, Cancer Research Technology Ltd and Babraham Bioscience Technology Ltd. Co-founder of Chiroscience in 1992.
CREATE Partners Limited www.createpartners.com	A fund management company that addresses the early stage funding gap between angels and mainstream venture capitalists and invests in companies focusing on emerging business opportunities. Create East of England Fund (£20m) since 2003 has made 29 investments across various sectors.
NW Brown Group Ltd www.nwbrown.co.uk	Founded in Cambridge in 1974. In 2003 it launched GEIF Ventures, a £5m co-investment fund to match investments made by business angels into high-growth companies. In 2006 it launched in partnership with two angel networks a £25m investment fund, IQ Capital Fund I LP, focused on early stage companies in high tech sectors. IQ Capital is part of the Enterprise Capital Fund (ECF) program.
Pentech Ventures www.pentechvc.com	Pentech Ventures focus on software infrastructure and applications, for internet content creation and management, communications, and for the new range of internet access devices. With offices in Scotland and London, Pentech invests prevalently in software companies in the UK and Eire.
Scottish Equity Partners (SEP) www.sep.co.uk	SEP is one of the largest VCs in Europe, with over £300M under management. With offices in Glasgow and London, SEP has specialist sector teams that focus on investments in information technology, healthcare & life sciences and energy related technology businesses. Last year, around 75% of SEP's investments were in early stage companies.

Other Organisations

Babraham Bioscience Technologies (BBT) Ltd www.babraham.co.uk	A wholly-owned trading company of the Babraham Institute. BBT was founded in 1996. The company exploits science and technology deriving from the Institute's research programs and takes responsibility for managing the patent portfolio.
East of England Development Agency (EEDA) www.eeda.org.uk	The East of England agency for sustainable economic growth and regeneration. Its task is to improve the region's economic performance and ensure the East of England remains one of the UK's top performing regions.
ERBI www.erbi.co.uk	Established in 1997 with a grant for 3 years from the DTI. As a networking organisation for Cambridge and the East of England, it provides a platform for biotechnology and related companies to interact. In 2000 ERBI became a private, not-for-profit, membership-based company with almost 300 members.
Skillcast Ltd www.skillcast.co.uk	A consultancy firm specialising in growing knowledge-driven sectors. It advises public bodies on innovation policy, commercialisation structures and funding. Skillcast has been involved in the setting up the Scottish Co-Investment Fund and helped raising an additional £25 million.
ITI Life Sciences www.itilifesciences.com	Established in 2003, ITI Life Sciences is one of the three Intermediary Technology Institutes (total investment £450M) set up in 2003 by Scottish Enterprise with the support of the Scottish Executive to identify and commercialise valuable technology-based intellectual assets.

Tables

Table 1: VC investment in European Countries - Absolute and relative values

VC Investment in 2004 (in € x 1,000) EVCA (2005)				
	Healthcare Medicare	%	Biotechnology	%
UK	1,071,393	35.6	171,234	24.9
Germany	744,591	25.6	150,461	21.9
France	233,294	10.8	143,524	20.9
Netherlands	218,240	6.9	24,367	3.5
Switzerland	24,418	1.1	17,173	2.5
Sweden	95,392	4.5	64,211	9.3
EU Total	2,801,209		686,617	

Source: EVCA (2005)

Table 2: Biotechnology and Pharmaceutical deals (Jan 2000-Sept 2006)

GOR	Deal count				Value (£000's)			
	VC Deal	Deal (non-institutional VC)	Other (Grant/charity)	Total	VC Deal	Deal (non-institutional VC)	Other (Grant/charity)	Total
East	144	24	21	189	566,325	86,229	5,008	657,562
East Midlands	13	4	2	19	9,930	1,268	70	11,268
London	52	13	14	79	192,420	12,520	6,973	211,913
North East	13	7	6	26	20,726	2,543	2,454	25,723
North West	24	4	5	33	103,649	1,030	1,270	105,949
Northern Ireland	4			4	1,775			1,775
Scotland	36	12	14	62	220,326	4,340	1,067	225,733
South East	70	15	7	92	357,790	13,410	1,630	372,830
South West	28	4	5	37	63,933	5,100	1,832	70,865
Wales	8	3	2	13	1,945	356	1,313	3,614
West Midlands	4		1	5	1,085		8	1,093
Yorkshire/Humber	24	5	4	33	11,060	12,540	1,382	24,982
Grand Total	420	91	81	592	1,550,964	139,336	23,007	1,713,307

Authors' calculation of *Library House* data based on authors regional coding

Table 3: Investment relative to regional GVA, 2000-2005 (ratios shown x1000)

GOR	Estimation of GVA basis	
	Work place	Residence
East of England	1.32	1.16
East Midlands	0.03	0.03
London	0.16	0.19
North East	0.11	0.13
North West	0.17	0.17
Northern Ireland	0.01	0.01
Scotland	0.51	0.51
South East	0.41	0.38
South West	0.12	0.12
Wales	0.01	0.01
West Midlands	0.00	0.01
Yorkshire	0.05	0.05
UK	0.23	0.23

Authors' calculation of *Library House* data based on authors regional coding

Table 4: Location of the nearest syndicate BVCA members

GOR	Deals with BVCA member involved	Percentage of all institutional VC deals	Deals with BVCA member in syndicate with an office:		No. of BVCA members with offices in region
			within same region	within the same or adjacent region	
East	98	71%	68%	99%	10
East Midlands	11	85%	55%	64%	5
London	23	44%	100%	100%	154
North East	10	77%	80%	90%	6
North West	17	71%	53%	65%	19
Northern Ireland	1	25%	100%	100%	4
Scotland	20	56%	55%	55%	17
South East	43	54%	30%	98%	13
South West	19	68%	58%	89%	7
Wales	4	50%	100%	100%	2
West Midlands	2	50%	100%	100%	13
Yorkshire	17	71%	82%	82%	8
Grand Total	265	63%	64%	90%	195

Authors' research of VC office locations based on Library House deals

Table 5: Biopharmaceutical investments made in counties in Golden Triangle Oxford - Cambridge - London 2000-Sept 2006

County	Deal		Deal (non-inst)		Other		Total	
	Count	Value	Count	Value	Count	Value	Count	Value
Cambridgeshire	121	469,677	20	85,345	17	4,318	158	559,340
Oxfordshire	38	231,546	3	5,010	2	400	43	236,956
London	52	192,420	13	12,520	14	6,973	79	211,913
Bedfordshire	5	2,625	1	-	1	-	7	2,625
Hertfordshire	4	3,087	-	-	-	-	4	3,087
Total	220	899,355	37	102,875	34	11,691	291	1,013,921

Authors' calculation of *Library House* data based on authors regional coding

Table 6: Average number of investors in local or adjacent regions per deal

GOR	Institutional deals		All deals	
	Local	Local or adjacent	Local	Local or adjacent
East	0.9	2.0	0.7	1.5
East Midlands	0.6	0.9	0.4	0.5
London	1.4	1.5	1.1	1.2
North East	0.6	0.6	0.3	0.4
North West	0.5	0.7	0.5	0.6
Northern Ireland	1.3	1.3	1.3	1.3
Scotland	0.8	0.9	0.6	0.6
South East	0.6	1.8	0.4	1.4
South West	0.5	0.8	0.4	0.6
Wales	1.2	1.2	0.9	0.9
West Midlands	0.6	0.8	0.5	0.7
Yorkshire	1.1	1.1	0.8	0.8
UK	0.9	1.5	0.6	1.1
Triangle	1.0	1.9	0.8	1.5

Authors' research of VC office locations based on Library House deals

Table 7: Institutional investment deals

Age (x) at time of round	Location of VC with respect to firm:		Total no. of deals	% of deals with VC in same region	% of deals with VC within adjacent region
	Same region	Same or adjacent region			
0 years < x <= 2 years	131	175	250	52%	70%
2 years < x <= 5 years	73	105	147	50%	71%
5 years < x <= 10 years	25	37	52	48%	71%
10 years < x <= 20 years	1	3	10	10%	30%
Total	230	320	459	50%	70%

Table is based on institutional investment deals (total of 463 deals) with named syndicate members available. VC location is based on the nearest office location of VC syndicate member. T-test confirms statistically significant difference between the proportion of proximate investors in 10-20 years group and other age groups - 5% level.

Table 8: Proximity of specialists (Jan 1996-Sept 2006)

GOR	Deals featuring specialist					
	Count of deals	Specialist in local region	Specialist in local or adjacent region	Specialist in local region and is an institutional VC	Any investor in local region	Any investor in local or adjacent region
East	86	48	84	42	62	85
East Midlands	1	0	0	0	0	1
London	37	30	30	20	36	36
North East	2	0	0	0	1	1
North West	14	2	2	0	4	6
Northern Ireland	0	0	0	0	0	0
Scotland	17	1	1	0	3	5
South East	34	6	29	2	17	32
South West	12	1	3	0	3	6
Wales	3	3	3	3	3	3
West Midlands	1	0	0	0	0	0
Yorkshire	8	4	4	2	5	5
Grand Total	215	95	156	69	134	180

Authors' calculation of *Library House* data

ⁱ This provided data on the names of investors and the amount of VC investment received as well as information on other forms of equity finance received during the history of the firm. The locations of firms were also cross-referenced with information from the FAME database, which provides details on SME in the UK, and company WebPages. All of the companies in the sample are based in the UK, whereas investors have HQs and offices worldwide. In addition we also collected data on the location of investors detailed in the database using information provided online by the British Venture Capital Association (BVCA) on their member's office locations, and by consulting the WebPages of active investment firms in our population of DBFs.

ⁱⁱ One exception to this is the North West, which has a higher level of investor proximity when specialist investors are found in the syndicate, although the specialists themselves are not local to the deal.

ⁱⁱⁱ Some DBFs, such as Cyclacel and Stemcell Science, implemented that strategy.