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Biobanks: instrumentation, personnel and cost analysis

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Key words

Tissue banks • Biobanking • Biological tissue conservation • Tissue cryopreservation • Description of costs

Description of costs

Instrumentation

Cryogenic systems

For rapid freezing of samples various methods can be used such as in prefreezed isopentane or immersion in liquid nitrogen (directly or vapour cooled). In the former case, isopentane can be kept in a dedicated container at -80°C, or a benchtop instrument can be utilised that maintains isopentane at the required temperature (e.g. Histobath®, Shandon). In the latter case, a liquid nitrogen container that respects current laboratory normatives is needed.

Labelling machines and bar-code readers

The best means to identify samples is with a one-or two-dimensional bar-code system. Pre labelled vials or labelling machines with inks and labels that are resistant to low temperatures can be used. Barcode readers should be interfaced with a computer system for easiest management: one reader should be positioned near the area where sampling of surgical specimens is performed, while another should be present where samples are stored. Readers are available using storage tubes with pre-printed two-dimensional barcodes, which permits the direct interface of the reader with a database, allowing easy tracking of samples (e.g. Trackmate and Easytrack2D, ThermoFisher).

Systems for cryopreservation

The choice of systems for cryopreservation of biological materials must be evaluated in relation to individual needs, the available space and the number of samples to be stored. It is possible to use electric freezers (-80°C) or liquid nitrogen storage systems that contain racks in which it is possible to place sample boxes. The number of freezers or liquid nitrogen tanks to acquire obviously depends on the expected volume of biomaterial, but also on the conservation strategy (e.g. storage of multiple aliquots of the same sample in different freezers) and the need to have emergency backup systems available. The capacity of a freezer or of a liquid nitrogen tank is based on the size of the instrument and the volume of each sample: for 2 ml vials, the capacity can vary from 10,000 to 35,000 vials; if one chooses conservation in cryomolds, then the capacity decreases by about one-half. If one has two medium-sized instruments and collects 500 cases per year, with 10-20 samples per case, (normal and pathological tissues plus biological liquids, using cryovials or cryomolds), then it can be estimated that the instrumentation will satisfy storage requirements for about 4-5 years.

Instruments should be connected to remote alarms to allow intervention in case of emergencies. Ideally, there should be a local alarm, a remote alarm that is under constant surveillance and an automatic dialer that can alert the system manager.

Individual protection devices are also needed in relation to whether freezers or liquid nitrogen tanks are utilised. For continuous refilling of liquid nitrogen tanks, it is best to choose a system that is connected to a fixed external station, or mobile containers connected to the tanks that are refilled periodically.

Instruments for the management of biological liquids

Whenever the management of biological liquids is performed directly at the biobank, a centrifuge is necessary for the separation of the various components (e.g. serum, plasma).

Instruments for quality control of biological samples

For quality control of samples, it is useful to have the appropriate instrumentation for measurement of the various biochemical components (DNA, RNA, protein) (e.g. Bioanalyzer, Agilent Biotechnologies).

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Systems for tissue microarrays

A workstation can be integrated into the biobank for preparation of tissue microarrays. In this case it is necessary to acquire the appropriate instrumentation, including a software, which can be interfaced with the management systems of the biobank.

Instruments for archiving

Since the biobank may also collect formalin-fixed, paraffin-embedded samples, in addition to frozen samples, racks and other equipment are needed for paraffin blocks and histological slides. For paper documentation, locking storage cupboards are needed.

Computerised support systems: hardware, software and web site maintenance

For archiving data and interfacing with management system in the Pathology Department, personal computers and software dedicated to the biobank are needed. The software must be able to manage three aspects: information relative to sample storage, pathological information and clinical data. Commercially available software is already available that meets these prerequisites that can be interfaced with the Pathology Department. It may be necessary to create an "ad hoc" system according to specific needs. In addition, software manufacturers of general managing systems for surgical pathology units are beginning to include a number of functions that are specific for data management for tissue banks. It may also be helpful to crate a web site containing information relative to protocols, type of material available and the means of access.

Personnel

For the optimal management of a biobank, in addition to the director, several key individuals are needed for quality control and technical duties such as collection and archiving of informed consent forms, patient information, biomaterials collection and database organisation. The quality control manager should possess a degree in medicine or biological sciences, and it is estimated that the individual would dedicate about 30-50% of his/her time in activities relative to the biobank.

Concerning patient data, collection of informed consent forms, checks of operating schedules theatres, and collection of all non-tissue samples a research nurse is necessary; for tissue collection, storage and manipulation of biomaterials, a full-time laboratory technician is needed. A part time secretary may be necessary to help out in data management as the number of samples increases. In this light, it is also worthwhile considered the possibility of forming a ethical/scientific committee that can evaluate requests for biomaterials.

Storage systems

For cryopreservation systems an appropriate space is required with: controlled temperature and ventilation, and monitoring of the partial pressure of oxygen in the case that containers for liquid nitrogen are utilised, the room should be easily accessible in terms of both daily use and maintenance. The size of the rooms needed depend on both the number and type of instrumentation adopted. Access to instrumentation should be controlled, preferably though electronic means.

Consumables

Cryovials, vacutainers, cryomolds, isopentane, tubes for blood samples

Depending on the type and quantity of materials that will be conserved (tissues to be stored in both cryomolds and cryovials, biological liquids) several types of containers are needed. For the collection of about 500 cases per year, the following can be envisaged over a 5-year period:

- 15,000 cryovials for the collection and storage of tissues;
- 10,000 cryomolds for collection and storage of frozen tissues in OCT;
- 7500 tubes for blood collection;
- 2500 sterile containers for urine collection;
- 32,500 cryovials for storing blood, serum, plasma;
- 7500 cryovials for urine storage;
- 7500 biocassettes;
- 20,000 microscope slides;
- 50 litres of isopentane.

If cryopreservation in liquid nitrogen is chosen, then the cost of liquid nitrogen must be added. The daily cost varies depending on the volume of the tank. For quality control of samples, the costs of reagents for extraction of biomolecules must be added (e.g. extraction of RNA).

Publications and formation of personnel

The activity of the biobank can be made known through publication in specialist journals and at scientific/medical congresses. In order to maintain a high operating standard, regular formative events should be organised for both medical and technical personnel.

Cost analysis and feasibility of the creation of a biobank in the Trentino region – Trentino Biobank (TB)

Following is a detailed analysis of a feasibility study for the creation of a biobank in the Trentino region in Italy within the framework of the local health system. The study was financed by a local foundation (Fondazione Cassa di Risparmio di Trento e Rovereto), and was carried out in collaboration with prof. Stefano Capri, Department of Economics, Università "Carlo Cattaneo" LIUC. The evaluation considered all the above-mentioned aspects, and put these in local economic terms for 2005-2006. Moreover, it was also considered that once the biobank was fully functional, it could make profit derived from the utilisation of biomaterials in specific research projects.

Variable costs and earnings

Infrastructure

The TB will be localized within a room of the Department of Pathology. Therefore, in real terms, the infrastructure itself does not pose any real costs as the structure is already available, and was thus considered as zero in economic terms.

Personnel

The participation of healthcare workers in biobanking activities was quantified only for individuals directly involved in the TB, those listed in Table I, which shows the foreseen percentages of time dedicated to the project over a 5-year period. The shift from part to full time for the nurse is relative to the increased number of patients and requests.
To calculate annual personnel costs, the following were considered as are listed in the hospital's balance sheets in 2006 at Santa Chiara Hospital (Tabs. I, II).

Instrumentation and equipment

Data are reported in Table III.

Disposables

Disposables were calculated for a 5-year period in proportion to the number of cases collected (Tab. IV).

General expenses

It is estimated that about € 4.300/year are needed for telephone expenses, travel, educational materials, etc.

Accounting

In the first year, the bulk of the expenses were dedicated to the acquisition of instrumentation and equipment, while personnel costs were minimal. Investments were considered as entirely financed in the acquisition period, and therefore contribute to the total yearly costs. However, as can be seen in the table, considered as a cost analysis, with the goal of obtaining an accounting statement, the impact of this investment in terms of depreciation shows reduced annual costs in terms of the balance sheet analysis.
Personnel costs begin to increase during the second year, and in the third year there are no new acquisitions of equipment. The total costs, including the entire annual equipment costs, go from € 231.210 in the first year to € 226.201 in the second year, and stabilise at € 144.749 for the third to fifth years.

Earnings

Economic profitability is not considered indispensable as the biobank is part of a research structure within a public hospital, with both diagnostic and research activities. However, it is interesting to simulate the possibility of profitability of the biobank over time, and receiving payment from third parties.
It is reasonable to hypothesise that requests for material from the biobank will increase with time. Such requests could initiate after the third year when the biobank is fully functioning, and could provide biological samples to third parties upon payment (laboratories, hospitals, pharmaceutical companies, universities). Market prices can be established, and profits can be expected that would cover the majority of the operating costs.
In quantifying the costs of each single request, it is useful to evaluate how much an analogous service costs from existing biobanks. The TuBaFrost project has considered this aspect in detail in document 6.3 [a]. According to that analysis, the cost of each frozen tissue sample should be from € 70 to € 100. In the US study described by the National Biospecimen Network Blueprint [b], adequate prices to compensate for the costs of management of biomaterials vary from $20 to $100 per sample when associated with accurate clinical data, and can increase up to $500 if molecular data is also included. Analogous data have been cited in a study by the National Cancer Institute and National Dialogue on Cancer [c]. Tissue microarrays produced from material in biobanks can also be sold to third parties. Similar tissue sections already on the market are priced from $20 to $350 per section depending on the number of samples contained within.
A more in-depth consideration of potential earnings is beyond the scope of the present study, and it is not possible at present to obtain a realistic evaluation as there is still insufficient experience in Italy in this regard.

Tab. I. Personnel of "Trentino Biobank".

	Year 1	Year 2	Year 3	Year 4	Year 5
Personnel					
Medical director	0,1	0,1	0,1	0,1	0,1
Research biologist	0,5	0,5	0,5	0,5	0,5
Nurse	0,5	1,0	1,0	1,0	1,0
Technician	1,0	1,0	1,0	1,0	1,0

[a] Deliverable D 6.3 Non-profit-making business plan for the European Human Frozen Tumor Tissue Bank project.

[b] Friede A, Grossman R, Hunt R, Li RM, Stern S, eds. *Biospecimen Network Blueprint*. Durham, NC: Constella Group, Inc. 2003.

[c] Human Tissue Repositories, http://www.rand.org/pubs/monographs/MG120/index.html

Tab. II. Annual personnel costs.

Role	Annual costs (1)
Medical director	131.109
Technician	43.896
Nurse.	45.501
Healthcare technician	43.396

(1) = relative to 2006

Tab. III. Instrumentation and equipment for "Trentino Biobank".

	Year 1	Year 2	Year 3	Year 4	Year 5
Containers for liquid nitrogen (1L)	197	–	–	–	–
LABPAL printer	935	–	–	–	–
Barcode reader	600	–	–	–	–
Cabinet for documentation	300	–	–	–	–
Server	–	4.000	–	–	–
Software MTT	95.000	–	–	–	–
-80 °C freezer	15.000	15.000	–	–	–
Equipment for tissue microarrays	–	52.000	–	–	–
Telephone alarms for freezer	350	350	–	–	–
Bioanalyzer for quality control	—	15.000	–	–	–
Histobath	7.200		–	–	–
Total	119.582	86.950	–	–	–

Tab. IV. Consumables in 5 years.

	Quantity	Unit cost	Total cost
Tape for LABPAL printer	78	25/m	1.950
Cryoracks	9	140	1.260
Boxes for cryoracks	17	69/10	621
Boxes for cryomolds	168	7,53	1.265
Cryovials	110	175/500	19.250
Cryomolds	15	109,14/1000	1.637
OCT	1		75/1275
Cassettes for slide and blocks			1.450
Secretarial expenses			1.500
Isopentane			500
Lymphoprep	30	70/500 ml	2.100
RNA extraction kits	3	885/250	2.565
EDTA vacutainers	7500	0,84	6.300
1% budget of consumables for Pathology Department (1)			20.000
Total			60.473

(1) = biocassettes, reagents, solvents, microtome blades, etc.

	Year 1	Year 2	Year 3	Year 4	Year 5
Cases collected	200	400	600	600	600
Costs of consumables (€)	5.498	10.995	16.493	16.493	16.493

Tab. V.

	Year 1	Year 2	Year 3	Year 4	Year 5
Investments	119.582	86.950	–	–	–
5-year depreciation	24.041	41.431	41.431	41.431	41.431
Total costs with depreciation	126.765	171.778	177.276	177.276	177.276

Conclusions

The costs of instrumentation and personnel of a tissue bank require adequate financial support. Only in this light is it possible to create a functional entity that can respond to the needs, normatives and high quality of biomaterials. Given the importance of the availability of biological materials for research purposes, originating from qualified and certified sources, healthcare budgets on a national and local levels should consider this fact. In this way, we should move ahead from a "do-it-yourself" tissue collection, as is most frequent at present, to a more professional service providing high quality material with potentially greater scientific impact.