

EDITORIAL

Swedish Oncology. Past – present – future

ULRIK RINGBORG

In 1974 the decision was made to reorganize the cancer care in Sweden. Several international investigations recommended the establishment of comprehensive cancer centers, which had been developed in many countries as complete cancer hospitals. In Sweden it was considered impossible to cover the cancer care with a limited number of cancer hospitals. Therefore a system of coordinated oncological centers was proposed and later implemented. The most active person behind this proposal was Jerzy Einhorn, at that time the Head of the Radiumhemmet, Karolinska Hospital. The oncologic clinics at the university hospitals received the mission of integrating the cancer care in a defined geographic area around the university hospital with the aim of using all the cancer care resources in a rational manner. The concept of multidisciplinary was established using the consensus document “The Care Program” as a tool with information and recommendations regarding diagnostic procedures, primary treatment and follow-up of cancer patients. Regional cancer registries were established and data on clinical stages, histopathology, primary treatment and follow-up were registered. Structures for screening programs were developed. Based on this activity the cancer program developed strongly during the following decades. The evidence based cancer care was a good basis for clinical research.

Over the past 15 years this organization has suffered from increasing problems. Economic restrictions as well as increased complexity in the cancer care have caused problems which have been difficult to handle with this form of organization, and which over time has fragmented. One important factor has been suboptimal leadership of the cancer care program, which in a number of clinics and hospitals is organized to support the traditional

organ oriented clinical specialties. The increasing cancer burden linked to economic restrictions escalates the fragmentation.

Cancer – a worldwide problem

No doubt, cancer is a global problem. In 2002 there were 10.9 million new cancer cases in the world and by 2020 16 million new cases are expected. In 2002 there were 6.7 million deaths due to cancer and 2020 the expected value is 10.3 million. In 2002 about 25 million people were living with a cancer diagnosis and the prevalence is increasing more than the incidence [1]. Thus, over time we have more new cancer patients. Due to improved treatments we have even more patients living with cancer. Over time we have identified more needs of the cancer patients. We must take into consideration that we are treating a human being suffering from all the consequences of a cancer, and not just treating an organ. Science offers us increasing innovations. This requires more interventions per patients. Presently cancer is the number two cause of death, second only to cardiovascular diseases. It is number one cause of death for individuals 75 years and younger.

Main strategies

There are two main strategies to meet present and future problems. A decreased incidence can only be achieved by prevention strategies. To overcome the problem with increasing number of patients living with chronic cancer disease the cure rate must be improved. This can only be done by an innovative cancer care, improved early detection and treatment.

Barriers to the development of innovative cancer care

The European cancer care is often criticized for being fragmented, a reason why Federation of European Cancer Societies, Organization of European Cancer Institutes and European Society of Medical Oncology have developed multidisciplinary strategic programs. We often have an insufficient global view of the patient. There is an increasing complexity and specialization and parallel to this we have serious economic restrictions. We often lack specialized staff. Due to successful research new diagnostic tools and treatment are increasing in number but often there are no systematic implementations of new methods. Analysis of the European countries shows variations in cancer treatment outcomes. This has been shown both in the European Code Against Cancer [2], a successful prevention program, and the EURO CARE a program which analyses survival after the diagnosis of cancer [3].

European cancer research is not free from criticism. Fragmentation is also a problem for the cancer research process. Funding is not coordinated and the iteration of research is a frequent phenomenon. There is a lack of coherence and insufficient collaboration. There is a general view that the cancer research has limited effects on cancer care and prevention. The European Commission tried to improve the European cancer research in the 6th Frame Program. Due to too small effects an extensive analysis of European cancer research (EUROCAN+PLUS) is now ongoing and will be reported to the European Commission at the end of 2007.

Sweden is not an exception. We also share the problems with the other European countries with a fragmented health care system and research organization. Therefore we have initiated activities with both local and national agencies to establish a national cancer plan. Such a plan must analyse and propose a prevention strategy with the aim to decrease the incidence of cancer. Equally important is action to follow the proposal by WHO to create comprehensiveness in the cancer care [4]. Comprehensiveness means integration of the health care with research and education with the aim of achieving innovative cancer care.

If innovation is an important goal the cancer research must undergo a detailed analysis. We have an extreme expansion of knowledge in basic research but at the same time there are numerous problems in the clinical research area with clinical trials serving as a bottleneck. There is a gap between basic and clinical research which must be bridged. We have difficulties

in implementing new knowledge into routine care. Also in Sweden, which has unusually good possibilities for developing patient databases, outcome research is only partially developed.

The cancer research process must be seen as a research continuum which is presently not the case. Information from basic research and tumour biology should be effectively transferred to preclinical and clinical research. Important research results from clinical trials should be implemented in clinical care and evaluated. The process of knowledge from basic research to clinical evaluation is fragmented. A time duration, which is often 10–20 years, is required for an important discovery to be implemented in routine care. This time frame is not acceptable and must be shortened. Translational research means a research continuum and if this concept is to be established we must avoid the problem of only a small percentage of patients being involved in clinical trials [5,6]. We must create an appropriate environment for translational research and increase multidisciplinary research collaboration. Translational research is focused on the cancer patients with transfer of information from bench to bedside but also from bedside to bench. The present funding systems should be more focused on translational research and multidisciplinary research collaboration and the educational systems should facilitate such a development.

Challenges

There are today spectacular opportunities for the improvement of cancer care. The following are a few examples:

Molecular genetics provides us with strong instruments for identifying high-risk individuals for prevention programs. The development of molecular pathology/cytology will change tumour classification, offer new possibilities for identifying patients with local or disseminated disease but also methods for predicting treatment response. Functional and molecular imaging will give the treatment specialities detailed information about tumour distribution but also be helpful in evaluating early treatment responses. Multimodal treatment will further be optimized towards organ preservation. Within radiation therapy both physical innovations and development of molecular radiobiology will improve and individualize treatment. Medical treatment is complex with development of targeted therapy, hormonal treatment, immunotherapy and gene therapy. Strategies for developing treatment result prediction and establish personalized medicine are under development with the use of biomarkers and systems biology.

Other important areas are psychosocial oncology, rehabilitation and different forms of supportive care.

Corner stones of organizing cancer activities

As a whole cancer is a very complexed area. Important corner stones in an organization are multidisciplinary, integration and the development of a critical mass.

A well developed multidisciplinary is a necessity if cancer care is to be of high quality. A number of subspecialties must be parts of or linked to the multidisciplinary teams. These include: prevention, pathology/cytology, imaging, laboratory medicine, surgical treatment, radiation therapy, medical oncology, psychosocial oncology, rehabilitation, supportive care and palliative oncology among others.

An important aspect of quality is innovation. A prerequisite for innovation is integration of prevention and care with research and education but also an integration of the cancer research process.

Another aspect is education which is also complex and includes basic education, specialist training, research education where MD/PhD programs are important, continuous medical education, education of patients and relatives as well as education of the general population and decision makers.

Over time the critical mass is increasingly becoming more important. An organization in which prevention, care, research, development and education are integrated is labelled a comprehensive cancer center. To afford the multidisciplinary for quality care and a reasonable research a population basis of 2–4 million inhabitants is needed. The way health care is organized today there are hospitals and clinics outside the comprehensive cancer center. In order to assure the quality of health care but also establish research collaboration it is important to create a network organization around the comprehensive cancer center. Due to increasing complexity with subgroups of cancer patients, rare diagnosis, expensive technologies and increasing demands for competence a single comprehensive cancer center cannot cover all types of cancer research. In order to reach a critical mass a network of harmonized comprehensive cancer centers should therefore be developed in Europe.

Important European activities

The Organization of European Cancer Institutes (OECI) is a non government and not for profit organization. It is a European Economic Interest Grouping which means it is a legal entity in the European Union [7]. At present the organization links 52 cancer institutes in Europe. The

organization has a common vision of future European Oncology including the concept of establishing comprehensiveness by integrating prevention and care with research and education. An important goal is to create networks of comprehensive cancer centers to share resources and reach the critical mass. OECI has a number of activities to reach this goal. Important is an Accreditation Program covering care and prevention as well as research and education. The program will help us to develop comprehensive cancer centers as cancer hospitals and/or virtual organizations. A second pilot project aimed at testing tools to measure infrastructures and assess quality together with an auditing procedure is ongoing and the methodology is planned to be ready for use during 2008. Other important OECI activities are working groups for education, clinical guidelines, biobanking with a virtual European tumour bank, biopathology and new technologies for radiation therapy and imaging. The working programs aim at supporting comprehensiveness in cancer centers.

There are other European activities which will in future also have an impact on Swedish oncology. Within the Federation of European Cancer Societies (FECS) there are plans to develop into one organization based on the concept of individual membership. The reason is the necessity for speaking to politicians and decision makers with one voice regarding cancer.

Within the European Organisation for Research and Treatment of Cancer (EORTC) a new strategy has been developed, (NOCI – Network of Core Institutions), a strategy to improve and facilitate biologically driven clinical trials. It is not enough to create networks of research teams in Europe but also collaboration must be enhanced between “Core Institutions” which means comprehensive cancer centers. This will provide the research teams with the necessary infrastructures for clinical trials which also includes biological questions.

The EUROCAN+PLUS Project originates from the European Parliament and the European Commission. The project analyses the background of the fragmented cancer research in Europe with identification of barriers and a proposal to overcome the fragmentation. Again, one of the conclusion from the project, which will be reported at the end of 2007, is the necessity for creating a network of harmonized comprehensive cancer centers in order to establish environments for translational research and overcome the problem of lack of critical mass.

In the 7th Frame Program special attention has been paid to infrastructures for translational research. There are several expensive structures needed like biobanks, well developed clinical trial

units, patient data registers and platforms for genomics and proteomics. These structures, if centers will be able to collaborate efficiently, shall be harmonized.

An important initiative in the 7th Frame Program is the Innovative Medicines Initiative (IMI), a collaboration between industry and academia. Many of the goals are shared by industry and academia. The development of new pharmaceuticals is extremely expensive. A collaboration regarding translational research in this area with sharing of knowledge and resources will most probably escalate the innovation of cancer care.

European strengths

The strong criticism regarding European cancer research must be balanced by mentioning important strengths. There is an unusually strong basic research platform in Europe, a platform of importance for the development of translational cancer research. Europe has important intellectual capital. In many countries population based patient materials are available and patient registers are well developed. There is also a strong potential for creating biobanks, in some countries population based tumour banks. Another good example is the Nordic serum banks [8]. There is a long-term strategy within the European Commission for stimulating European collaboration by coordinating funding for cancer research.

Stockholm Academic Health Care System – the Karolinska Comprehensive Cancer Center

In Stockholm a program has been initiated which will improve integration of health care with research and education, the Stockholm Academic Health Care System. This is a strategy to overcome the divided ownership of health care and academic activities, the former owned by the county and the latter by the state. The new Karolinska University Hospital will in the future focus more on highly specialized health care and innovation. The basis is translational medicine. A part of the program is the development of a more visible and functional comprehensive cancer center. The objectives for such a center are multidisciplinary, integration of the research process but also reaching a critical mass. With a population of 2 million inhabitants it is important to develop collaboration with other national and international cancer centers. The project developing a comprehensive cancer center in the new health care structure has been active for one year. The main focus is on the development of infrastructures for translational research. A number

of subprojects have been launched. A clinical trial structure will be extended to cover the whole Karolinska and to a larger extent support biologically driven clinical trials. There presently exists a biobank project for all medical disciplines. In one subproject work is ongoing to make the tumour bank complete and involve normal tissue from cancer patients. A link has been created to the European virtual biobank, TuBaFrost, which at present connects 11 European cancer centers [9]. There are good population based patient data registers but they should be extended to be more detailed. A separate program has been set up to prospectively register not only primary treatment and follow-up but also treatments of recurrent disease and outcomes. The different structures for genomics/proteomics are the subject for a subproject aiming at a rational collaboration. A bridge has been created to the Human Proteome Resource at the Royal School of Technology [10]. The latter is a spectacular program to identify important proteins and provide clinical researchers with antibodies. A strong program has been initiated to implement systems biology into the clinical research with the aim to personalize the cancer treatment. Other important structures under development are those for molecular pathology/cytology, oncologic pharmacology, preclinical research structures, cancer nursing, palliative oncology, quality of life assessment, psychosocial oncology, rehabilitation and health economy.

Education is another important area. Analysis has started with the aim to integrate basic training of physicians to provide new doctors with an education more focusing on multidisciplinary in cancer care. Specialist training of nurses in different fields of oncology is another subject for education.

Networking

It will be impossible to reach the critical mass for a large part of oncologic research unless collaborative networks are established. It is therefore important to provide different centers with the harmonized infrastructures for translational cancer research. Networks should be created, not only between research teams but also cancer centers. Many of the infrastructures needed for translational cancer research cannot be established by the research groups but need the support from the decision makers in the cancer centers. A large part of future clinical research needs a holistic view of the cancer patients in order to integrate clinical activities needed for a cancer patient. It is important to share this view within the country in order to link the centers located at the university hospitals. It is also important to establish a network around the university

hospitals in order to assure the quality of cancer care but also to involve patients in clinical trials. With the increasing complexity in cancer research an international collaboration is mandatory. This is the background to the different European activities stimulating collaboration between cancer centers. Again, harmonization of infrastructures in the centers is a necessity if the research groups will be able to optimize collaboration.

With this background several countries have developed national collaborative organizations to link cancer centers. In France the French Federation of comprehensive cancer centers links such centers to create a national platform for development of cancer care and research [11]. In UK extensive reorganizations of the cancer care and research has been the fruits of a national cancer plan [12]. Again an important focus is a national translational research network. A similar development is seen in Italy with the *Alleanza Contro il Cancro* [13]. In Sweden no such organization exists. If a national platform will be created a formal collaboration should be established between the centers in order to use all existing structures in a more functional way.

Conclusion

Coming back to the reorganization of Swedish cancer care 1974. This reorganization was built on a vision to establish multidisciplinary in the cancer care and create a basis for development of comprehensiveness. At that time the possibility of building comprehensive cancer centers as cancer hospitals was excluded. The coordinated cancer centers were at the beginning very effective in creating multidisciplinary with obvious positive effects on treatment outcomes of cancer patients [14]. Over time we have experienced a number of threats due to increased complexity but also economic restrictions. Therefore we are presently in a situation where inequalities exist above all with regards to the management of patients with recurrent disease [15]. Furthermore, the research process has increased in complexity and the need for translational research has over time become more evident. An

important step is therefore to find ways to integrate the research process and also improve the collaboration with the health care system. A fairly new need is that of the critical mass. The increasing subgrouping of patients as well as needs for biological material, expensive research techniques and intellectual capital make every center too small. One of the most important problems today is therefore to establish centers which are harmonized regarding infrastructures with the aim of facilitating both national and international cancer research collaboration, a collaboration in which the needs of the patients are in focus.

References

- [1] Stewart BW, Kleihues P. World Cancer Report. International Agency for Research on Cancer. Lyon: WHO; 2003.
- [2] Boyle P, d'Onofrio A, Maisonneuve P, Severi G, Robertson C, Tubiana M, et al. Measuring progress against cancer in Europe: Has the 15% decline targeted for 2000 come about? *Ann Oncol* 2003;14:1312–25.
- [3] Survival of cancer patients in Europe: The EURO CARE-3 Study. *Ann Oncol* 2003;14(Suppl 5).
- [4] WHO National Cancer Control Planning. International Union Against Cancer. 2004.
- [5] Ward LC, Felding JW, Dunn JA, Kelly KA. The selection of cases for randomised trials: A registry survey of concurrent trial and non-trial patients. *British Stomach Cancer Group. Br J Cancer* 1992;66:943–50.
- [6] Tejeda HA, Green SB, Trimble EL, Ford L, High JL, Ungerleider RS, et al. Representation of African-Americans, Hispanics, and whites in National Cancer Institute cancer treatment trials. *J Natl Cancer Inst* 1996;88:812–6.
- [7] <http://www.oeci-eeig.org>
- [8] Pukkala E, Andersen A, Berglund G, Gislefoss R, Gudnason V, Hallmans G, et al. Nordic biological specimen banks as basis for studies of cancer causes and control – more than 2 million sample donors, 25 million person years and 100 000 prospective cancers. *Acta Oncol* 2007;46:286–307.
- [9] <http://www.tubafrost.org>
- [10] <http://researchprojects.kth.se>
- [11] <http://www.fnclcc.fr>
- [12] <http://www.cancerresearchuk.org>
- [13] <http://www.e-oncology.it>
- [14] Talbäck M, Stenbeck M, Rosén M, Barlow L, Glimelius B. Cancer survival in Sweden 1960–1998. *Acta Oncol* 2003;42: 637–59.
- [15] Johansen C. Rehabilitation of cancer patients – research perspectives. *Acta Oncol* 2007;46:441–5.