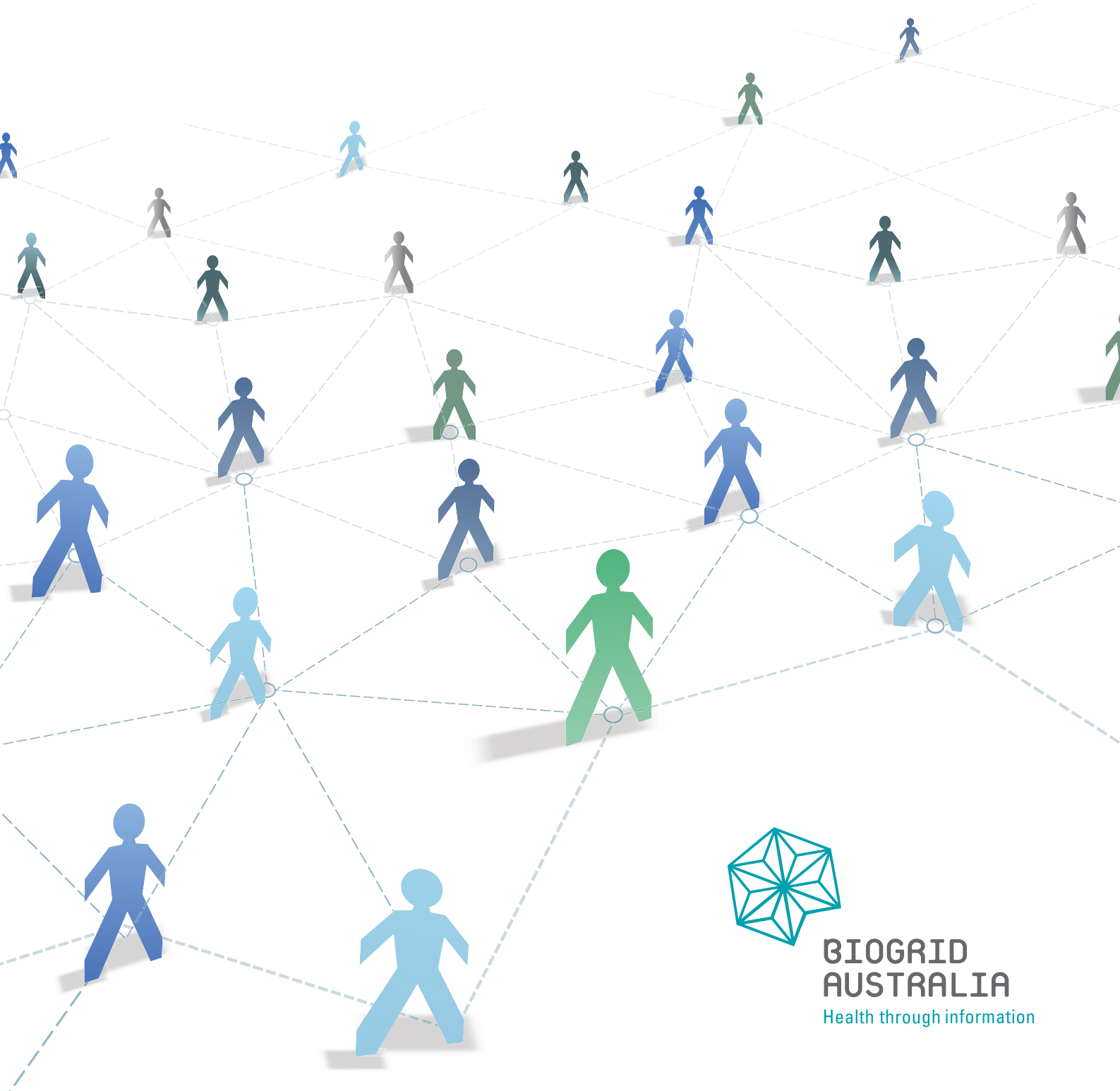
Advancing health research through collaboration

RESEARCH REPORT 2010



BIOGRID AUSTRALIA

Health through information

BioGrid Members[1]

ACT Health
Canberra Hospital

Adelaide Health Service (Central Northern Adelaide Health Service)
Royal Adelaide Hospital
The Queen Elizabeth Hospital
Lyell McEwin Hospital

Alfred Health
The Alfred
Caulfield Hospital
Sandringham Hospital

Austin Health
Austin Hospital
Heidelberg Repatriation Hospital

Ballarat Health Services
Ballarat Base Hospital
Queen Elizabeth Centre

Barwon Health
Geelong Hospital

Bendigo Health
Bendigo Hospital

Eastern Health
Angliss Hospital
Box Hill Hospital
Healesville Hospital
Maroondah Hospital

Goulburn Valley Health
Goulburn Valley Hospital

Latrobe Regional Hospital

Ludwig Institute for Cancer Research

Melbourne Health
The Royal Melbourne Hospital

Northern Health
The Northern Hospital

Peninsula Health
Frankston Hospital
Rosebud Hospital

Peter MacCallum Cancer Centre

Radiation Oncology Victoria

Southern Health
Monash Medical Centre, Clayton
Monash Medical Centre, Moorabbin
Casey Hospital
Dandenong Hospital

St Vincent's Hospital, Melbourne

Tasmanian Government Department of Health and Human Services
Royal Hobart Hospital
Launceston General Hospital

The Royal Children's Hospital

The Royal Women's Hospital

The University of Melbourne

The University of New South Wales

The Walter and Eliza Hall Institute of Medical Research

Western Health
Western Hospital
Sunshine Hospital
The Williamstown Hospital

[1] BioGrid member names and associated institutions as at 31 December 2010.

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About BioGrid

BioGrid Australia Limited is a secure research platform and infrastructure that provides access to real-time clinical, imaging and biospecimen data across jurisdictions, institutions and diseases. The web-based platform provides ethical access while protecting both privacy and intellectual property.

BioGrid was established in 2003 with the foresight of the Bio21 Cluster collaboration as the Molecular Medicine Informatics Model. Government funding has enabled the establishment then expansion of the platform over various phases.

- Phase 1 - 2003 - Victorian State Government Department of Innovation, Industry and Regional Development (now known as Department of Business and Innovation)
- Phase 2 - 2005 - Australian Government Department of Education, Science and Training (now known as Department of Innovation, Industry, Science and Research)
- Phase 3 - 2006 - Victorian State Government Department of Innovation, Industry and Regional Development (now known as Department of Business and Innovation (DBI))

BioGrid is now an independent not-for-profit company owned by 25 collaborators representing 41 hospitals and research organisations across five states and territories.

As modern research and planning becomes more complex, the need for collaboration in research significantly increases. The web-based platform has the capacity to uniquely identify and ethically integrate data collected about a consumer across multiple institutions.

BioGrid also has the capability to link data with other datasets, produce tailored reports for auditing and reporting and provide statistical analysis tools to conduct more advanced research analysis. Authorised users can access, transform and add to data and test research questions using their own analytical tools or those made available by BioGrid.

In its first full financial year operating as a company, BioGrid has continued to expand the Australian Cancer Grid funded by DBI and support research across a range of disease types and health areas. As at December 2010, patient records linked to BioGrid are over 195,000 and 64 databases have been linked with many more either in development or on track to link in the near future.

For more information on what data is linked to BioGrid and how to access data, go to **www.biogrid.org.au**.

BioGrid Vision

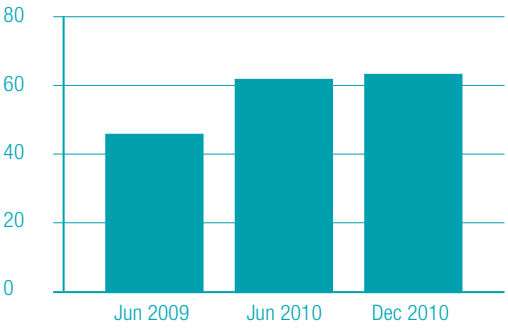
Integrating health and research data to facilitate improved health outcomes.

BioGrid Mission

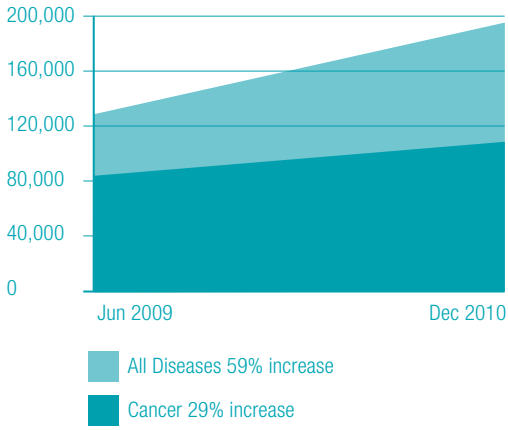
Providing a technology platform for the ethical integration of data from individuals, health services, industry, research organisations and governments for research to reduce the burden of disease and improve human health.

Growth Statistics

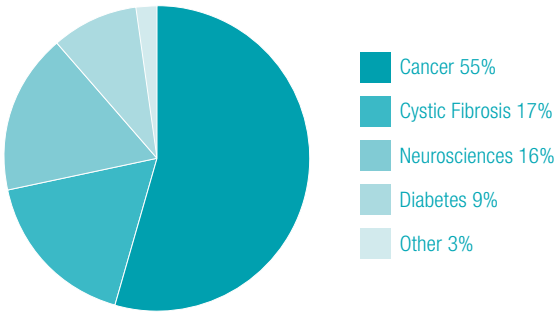
Number of databases linked to BioGrid



Number of privacy-protected patient records



Type of databases linked to BioGrid at December 2010



Supported by

A Victorian Government initiative
Victoria The Place To Be
Department of Business and Innovation

Victorian Cancer Agency
Linking research and patient care

Australian Government
Department of Innovation, Industry, Science and Research

Chief Executive Officer's Report

As Chief Executive Officer of BioGrid Australia, I am pleased to present the Research Report for 2010. Reflecting on the past 12 months, it has been a busy and challenging time for BioGrid as it transitions from a fully funded government project to a business providing data services to the health research sector. The focus of the Board and executive management team has been on developing financial sustainability for BioGrid post the Australian Cancer Grid Government funding. During the year income from research grants and retrospective pharmaceutical sector research studies has supported the business plan of generating revenue from multiple income streams and members voted to introduce membership fees effective 1st July 2010 to assist with ongoing sustainability of BioGrid.

The strategic direction of the business is to focus on further developing data linkage in major cancers such as Bowel, Breast, Lung and Prostate cancer. In addition, where project funding is provided, further data linkage in other disease areas such as Diabetes, Neurological and Respiratory will be developed.

There have been a number of highlights and achievements over the past year that should be acknowledged.

Launch of CART-WHEEL.org

Professor Sir Gustav Nossal launched CART-WHEEL.org (Center for Analysis of Rare Tumours) on 14 April 2010. Funded by the Victorian Cancer Agency this consumer grant has enabled a world-first website to be developed providing an ethically approved web portal for consumer driven research into rare tumours and molecular sub-types of common tumours.

Government Datasets

Significant progress was made during the year to gain access to externally linked data with the Australian Institute of Health & Welfare Death Index and the Victorian Admitted Episodes Dataset. Opportunities to link with other government datasets are being pursued. When these linkages are achieved it will significantly increase the value of BioGrid to the researcher.

Strategic Relationships

The directors and management have been developing strategic relationships with potential future users of the BioGrid platform to underpin key research initiatives such as the Victorian Comprehensive Cancer Centre, the Monash Comprehensive Cancer Consortium and the Olivia Newton-John Cancer and Wellness Centre.

International Cancer Informatics

There has been ongoing liaison with the National Cancer Research Institute Informatics Initiative, UK and the National Cancer Institute's caBIG (Cancer Biomedical Informatics Grid) initiative, USA. Future collaboration will provide opportunities for Australian cancer researchers to understand international trends in clinical informatics, with access to additional tools and data.

The successes of the company have largely been due to the many people who have contributed to BioGrid. Firstly on behalf of the company Board, executive management team and the member's Management Committee, I would like to thank the Victorian Government Department of Innovation Industry and Regional Development (now known as Department of Business and Innovation) for their engagement with BioGrid and their funding of the Australian Cancer Grid project until June 2011.

Since 2003 Melbourne Health has continued to act as Secretariat and home for the Australian Cancer Grid project. The continued support for BioGrid from the Melbourne Health executive team is greatly valued and appreciated.

I would like to acknowledge the commitment and dedication of the executive management team, Ms Maureen Turner (General Manager), Associate Professor Peter Gibbs (Clinical Director) and Dr Marienne Hibbert (Project Director) for their dedication and commitment to the ongoing development of BioGrid. The contributions and cooperative work of the Australian Cancer Grid Project Board, the member Management Committee and the Scientific Advisory Committees over the past year has also been a great support to BioGrid.

Finally, I take the opportunity to thank all the BioGrid staff for their enormous dedication to the company. Through what has been a challenging time with a considerable reduction in staff numbers, all staff have focused upon delivering real progress in facilitating the delivery of quality health research. With BioGrid's new structure having been implemented we are now in a robust position to capitalise on the opportunities that the coming year holds.

Mr Bob Atwill
Chief Executive Officer, BioGrid Australia

Clinical Director's Report

In my roles of Clinical Director of BioGrid Australia and Chairman of the BioGrid Scientific Advisory Committee (SAC), the past 12 months have seen continued expansion with the addition of new sites, new tumour types and disease areas, and greater research output. Being involved with BioGrid since its inception, as a founding clinical researcher, my role has been to generate increasing engagement from clinicians and industry with a goal of developing data collection across a broad spectrum of diseases, with the long term aim of improving clinical outcomes for patients.

Meeting quarterly throughout the year, the Cancer SAC comprises representatives from member organisations and affiliates who have expertise in particular tumour stream areas. A Life Sciences SAC was established in 2010 to ensure member representation in relation to other disease areas. The role of the SAC's is to lead and oversee the rapidly expanding and evolving science and research activities of BioGrid, including reviewing and approving data access requests from researchers.

In late 2010 a Pharmaceutical Advisory Committee was formed to lead and oversee the validity of commercial activities of the company to ensure that projects are aligned with BioGrid's strategy such that industry can support research activities without compromising any of our core values. Members of the advisory group include clinicians, researchers, members of the executive management team and external commercial expertise.

A number of important activities supporting research were achieved during the past year of which two are highlighted below.

Roche Collaboration

This significant study between BioGrid and Roche Products continued to progress in 2010. The study focuses on Bowel cancer treatment decision making and building on the already established data collection and analysis resources of BioGrid in this tumour stream, collecting data on up to 1,000 patients across Australia. Using BioGrid technology, the project will provide insight into how clinicians choose from the multiple potential treatment options available for patients with advanced Bowel cancer.

New ACCORD Modules

There has been significant development during the past 12 months with the completion of multiple new ACCORD (Australian Comprehensive Cancer and Research Database) modules namely; Breast, Prostate and Renal cancer, and Chronic Lymphocytic Leukaemia. The increasing level of clinician interest in ACCORD has resulted in the software being installed at many new institutions, with clinicians now collecting and entering data at these new sites. Over time as the number of patients entered increases and with maturity of the data these new sites will be major contributors to the research output enabled by BioGrid.

Research activities in the non-cancer area of life sciences also achieved major results throughout the year. Separate studies into Diabetes and Cystic Fibrosis data resulted in evaluation of different aspects of care and treatment plans benefiting patients. A world-first study comparing the outcomes of anti-epileptic drug therapy was conducted with the findings recently being published in the journal, *Neurology.*

Research output from Colorectal data continues with multiple publications related to clinical data, and also combining data and tissue based research, across a range of topics. The first publications are also appearing related to the brain tumour database, with multiple research projects underway across a broad spectrum of malignancies where data on substantial numbers of patients has now been collected with the support of BioGrid.

Along with the interest of industry in data collected as part of the standard ACCORD cancer datasets, there has been increasing enthusiasm from pharmaceutical companies in supporting prospective data collection projects that address specific questions related to clinician decision making, and treatment selection and outcomes in routine practice. These projects while addressing often quite specific questions, are also supporting capture of our standard dataset. With each of these projects being developed with a national vision they will not only provide a revenue stream that is critical to support and expand data capture and research, but also will create additional interest and engagement in BioGrid across Australia.

I would like to take this opportunity to acknowledge the commitment and contribution of the Scientific Advisory Committees over the past year. I would also like to thank all the clinical leaders and researchers for their hard work and perseverance during the year, and the BioGrid team members for their ongoing support.

Associate Professor Peter Gibbs
Clinical Director, BioGrid Australia

Project Director's Report

The Australian Cancer Grid (ACG) project completed a number of major milestones in 2010, increasing the research capacity in Australia and helping member participation in research projects. This phase is funded by the Victorian Government Department of Innovation, Industry and Regional Development (now known as Department of Business and Innovation) until 30 June 2011. The BioGrid technology data platform now extends to 41 institutions across metropolitan and regional Victoria, as well as Tasmania, South Australia, Australian Capital Territory and New South Wales. The past 18 months (June 2009 to December 2010) have seen an expansion of connectivity within member institutions (by 40%) resulting in a 39% increase in databases linked and a 60% increase in privacy-protected patient records.

The BioGrid platform is currently being used for research studies in Cancer, Diabetes, Epilepsy and Cystic Fibrosis and is being considered by researchers in other disease areas such as cardiovascular disease, respiratory medicine, mental health, and infectious diseases.

The BioGrid team has worked very hard to achieve a number of additional successes utilising the BioGrid technology and these are highlighted below.

Clinical Viewer Project

Development of a web based portal (Clinical Viewer), which allows authorised clinicians treating the same patient for the same disease across a number of sites and medical disciplines to view relevant identified patient information from outside an institution. This project was made possible by the support of the Western and Central Melbourne Integrated Cancer Service.

On-line Learning Modules

Learning how to access and utilise data in BioGrid has been made easier by the development of on-line learning modules now available via the BioGrid website. These modules, funded by the Victorian Cancer Agency, will be valuable reference tools for researchers.

Clinical Fellowships were awarded by the Victorian Cancer Agency to researchers working with BioGrid including Drs Jayesh Desai and Jeanne Tie from the Ludwig Institute for Cancer Research, and Dr Clare Scott from The Walter and Eliza Hall Institute of Medical Research. Dr Desai will focus on developing new therapies for Bowel cancer and Sarcoma patients, Dr Tie will study the use of a new biomarker to detect Colorectal cancer and Dr Scott, will conduct further research into an aggressive form of Ovarian cancer. The Sarcoma and Ovarian studies will use the BioGrid developed CART-WHEEL.org database in their research. The Colorectal biomarker studies will use BioGrid as the mechanism to capture and link clinical data across multiple sites.

Throughout 2010 BioGrid has focussed on a number of key cancer streams; however BioGrid's proven data platform and infrastructure has continued to provide opportunities for research in other disease areas. In addition to the reports published, projects in other areas are progressing, and new substantial projects are expected to be initiated over the next year or two.

I would like to thank the many people who have helped BioGrid have another successful year; the researchers, the members, and the Scientific Advisory Committees, who have all continued to champion and drive BioGrid enabled research, and the BioGrid team whose hard work and dedication keep the complex BioGrid system growing. Detailed reports on achievements and activity across the cancer streams and other disease areas for 2010 can be found in the Research Report commencing on page 7.

Dr Marienne Hibbert
Project Director, BioGrid Australia

Research Reports: Cancer

Bone and Soft Tissue (Sarcoma)

Dr Jayesh Desai is the BioGrid Bone and Soft Tissue tumour stream leader. Dr Desai is a Medical Oncologist at The Royal Melbourne Hospital and Peter MacCallum Cancer Centre and Senior Research Staff at the Ludwig Institute for Cancer Research. He is the Deputy-Chair of the Australasian Sarcoma Study Group (ASSG).

Background

Sarcomas are a diverse group of malignant tumours that develop from Bone and Soft tissues (fat, muscle, nerves and blood vessels). Although rare; they comprise about 1% of adult and 15% of paediatric malignancies. The morbidity and community impact of Sarcomas is significant given the high proportion of younger people affected compared to most other solid tumours. For example it has been estimated that 17 years of life are lost per Sarcoma diagnosis, three times the rate for Bowel or Breast cancer.

Progress and Challenges

Over the past 12 months, we have made ongoing progress with implementing data collection at each of the ASSG sites. The ACCORD[1] Sarcoma database was built, tested and data collection has been underway at the Peter MacCallum Cancer Centre since July 2009. Database installation and data entry has been progressively rolled out to all participating ASSG sites, with data now collected at all sites in Victoria, New South Wales, Queensland, South Australia, Western Australia and Austalian Capital Territory using the ACCORD database or equivalent. Data on over 700 patients has now been collected. Linkage through BioGrid has been established at Peter MacCallum; progress is ongoing at remaining sites. Funding for data collection at each site has been provided by ASSG, supported by a grant through Cancer Australia, with matched funding provided by the sites.

A Sarcoma Database Users Group has been formed and data managers attended a training meeting coordinated with BioGrid in May 2010, where members met and discussed data collection processes at each site, reporting requirements and issues for resolution. Members were introduced to BioGrid and received 'hands-on' training for ACCORD (data collection), SAS Web Report Studio (reporting) and SAS Enterprise Guide (querying). An evaluation of this meeting showed that the event was a success and worthwhile holding again; specifically, participants found meeting fellow data managers particularly useful for sharing common issues and methods of data collection while the technical element was also welcomed as useful for resolving questions and demonstrating reporting capabilities.

Discussion and collaboration with the Cancer Australia Chair for Cancer Epidemiology, Professor David Roder, to provide high quality clinical data to enable comparison between Australian epidemiological data and data about clinical care and standards data against international benchmarks continue.

A clear challenge identified early in the development of the Sarcoma database initiative related to the complexity of quality data collection given this is really a diverse set of diseases. Referral of patients to specialist centres of care, with an ongoing shared-care arrangement adds to the challenge of tracking patient outcomes. Leveraged funding and support for ongoing data collection through the ASSG will continue into 2011, an approach that has been successful to date.

Future Directions

High quality clinical and epidemiological data and mapping patterns of care will be available at all sites over the next 12 months. Discussions are ongoing for paediatric data collection, and to address specific issues with the AYA population. A specific research project that is being developed relates to evaluating outcomes in patients who have had resection of lung metastases from sarcomas, including QOL (collaboration with PoCOG). The clinical data for this study will be collected via the ACCORD database, the appropriate modifications have been made to enable this. Further prospective studies are in development.

[1] Australian Comprehensive Cancer and Research Database.

Breast

Associate Professor Clare Scott is the BioGrid Breast tumour stream leader. She is a Medical Oncologist at The Royal Melbourne Hospital and The Royal Women's Hospital and Laboratory Head at The Walter and Eliza Hall Institute of Medical Research.

Background

Breast cancer is the most common invasive cancer among Australian women and the second most common cancer causing death after Lung cancer. It is uncommon in males. Getting older is the most common risk factor: about 13% of new cases are among women aged 20-44, 61% in women aged 45-69 and 26% among women over 70. Women of all ages need to understand the importance of finding and treating Breast cancer early.

Fifteen per cent of all Breast cancers are advanced at diagnosis. Women whose cancer is diagnosed when it is contained in the Breast, have a 90% chance of surviving five years compared with a 20% five-year survival when the cancer has spread at diagnosis.

Progress and Challenges

There are several projects at a state level that have a direct link to the Breast tumour stream.

1. The Cancer Council Victoria (CCV) along with Western and Central Melbourne Integrated Cancer Service (WCMICS) has developed a Victorian Consensus Dataset (VCDS) for the Breast tumour stream. This published/online dataset (http://www.cancervic.org.au/downloads/cec/VCDS-project/VCDS-Breast-Data-Set.pdf) will provide the opportunity for data to be collected in a uniform and standard manner across Victoria. BioGrid has developed an ACCORD module for Breast cancer data collection, based on the VCDS dataset. This module is widely applicable for sites with standard access database capability. This has enabled prospective data to be collected at three Victorian sites (Austin Health, Box Hill Hospital and Monash Medical Centre) and additional sites have expressed an interest in using this database.
2. The CCV and WCMICS project entitled RUTH, is establishing software at four hospitals in Melbourne to assist in clinical treatment of patients. BioGrid has representation on the governance committee for the RUTH project. RUTH is now in use for collection of data, with active multi-disciplinary meeting capability.

Future Directions

To continue to develop the Breast ACCORD module with the following functionality for managing Breast cancer patients will be the focus in the future:

- Generation of letters to GP's;
- Functionality to support the multidisciplinary team; and
- An intranet accessible prescribing capability as part of the BioGrid electronic chemotherapy prescribing module, with linkages to EviQ.

Central Nervous System

Dr Kate Drummond is the BioGrid Central Nervous System (CNS) tumour stream leader and a Consultant Neurosurgeon at The Royal Melbourne Hospital.

Background

CNS tumours comprise a wide variety of tumour types and data is collected on all patients having neoplastic brain lesions removed, with tissue also collected and banked. Of these tumour types, glial tumours and metastases are both common and are associated with a poor prognosis, and thus are a particular focus. Data collected on cerebral metastases has obvious synergy for data linkage with other primary cancer databases through BioGrid.

Progress and Challenges

Over 2010/11 the paper-based data collection has been replaced with web-based electronic data collection and the processes for obtaining follow-up and survival data have been streamlined, including access to the Victorian Cancer Registry to complete survival data. Increasing use of the data has led to a reappraisal of some of the data fields, particularly when there are multiple tumours, and has suggested some expansions, particularly for molecular pathology data. Thus, an upgrade of the database is planned.

The database now contains over 2,000 patients and is being used for a number of collaborative projects looking at biomarkers in malignant glioma, the characteristics of long-term survivors from glioblastoma multiforme, tumour-associated Epilepsy and treatment pathways in patients with Lung cancer and Brain metastases. Abstracts have been accepted at national and international meetings and initial publications have been accepted. Interest has been expressed by a number of Australian groups to use the database format, but funding and manpower remain significant issues for those groups who do not routinely collect tumour data.

Future Directions

Completion of a number of the projects listed above will be a priority. Use of the database has commenced in Adelaide and future expansion is planned.

Presentations and Publications

Publications

1. Multidisciplinary Team meetings in Neuro-Oncology; Communication and Clinician Satisfaction. K Field, M Rosenthal, J Dimou, M Fleet, K Drummond. *Journal of Clinical Neuroscience*, Accepted June 2010.

Presentations

1. Pre-operative blood parameters as biomarkers for high grade gliomas. K Field, M A Rosenthal, P Gibbs, T Wohlers, K Drummond. Poster presentation, American Society of Clinical Oncology Annual Meeting June 2010.
2. Using a prospective comprehensive database to define features that impact the outcome of patients with Glioblastoma Multiforme. K Field, M A Rosenthal, S Kosmider, P Gibbs, K Drummond. Poster presentation, American Society of Clinical Oncology Annual Meeting June 2010.

Chronic Lymphocytic Leukaemia

Dr Constantine Tam is the BioGrid Chronic Lymphocytic Leukaemia (CLL) tumour stream leader. Dr Tam is a Haematologist at St Vincent's Hospital Melbourne, and a member of the CLL Australian Research Consortium (CLL-ARC), a collaborative body of enthusiastic CLL clinicians and researchers dedicated to finding the cure for CLL. His responsibilities within the CLL-ARC are to facilitate the establishment of a comprehensive, multi-centre clinical data network and to develop the next generation of treatments for CLL to be tested in clinical trials in Australia.

Background

Chronic Lymphocytic Leukaemia (CLL) is a type of slow growing Leukaemia that affects developing *B-lymphocytes* (specialised white blood cells). Under normal conditions they produce immunoglobulins (also called antibodies) that help protect our bodies against infection and disease. In people with CLL, lymphocytes undergo a malignant (cancerous) change and become leukaemic cells. CLL is the most common adult Leukaemia in Australia (with the diagnosis made in 700 patients each year[1]), and yet little is known about its cause, and it is not curable with current technology.

For many people CLL remains stable for many months and years and has little if any impact on their lifestyle or general health. Around 50% of people diagnosed with CLL never require any treatment for their disease and can survive for many years despite their diagnosis. For others, the leukaemic cells multiply in an uncontrolled way. It is not known why the Leukaemia is so indolent in some patients, and aggressive and life-threatening in others. More research is required to understand the genetics of CLL, in order to find weaknesses in the cancer that can be exploited by new drugs. By better understanding what causes the Leukaemia to be aggressive and what its weaknesses are, we hope to construct treatment programs that can cure CLL.

Progress and Challenges

Historically patient datasets have been collected in many research institutions (e.g. St Vincent's Hospital and Royal North Shore Hospital) but standard datasets have never been defined, and these datasets have never been linked or analysed in a systematic manner. BioGrid will facilitate the linkage of a standard dataset using ACCORD and other databases to make the data available to researchers and clinicians in a de-identified manner. Development of the CLL module in ACCORD has been completed, with support from Roche.

The CLL module in ACCORD has been installed with data currently being collected at St Vincent's Hospital as the lead site for this collaborative project.

Future Directions

Once the CLL module is active at St Vincent's Hospital, the historical data at this site will be entered into ACCORD as a final check on the function and integrity of the system. The ACCORD module will then be rolled out to interested CLL-ARC sites in order to establish a nationwide, comprehensive network.

The initial research projects will be devoted to understanding the epidemiology of CLL within the Australian population and how differing treatment practices influence major outcomes such as response to chemotherapy, side effects and survival. We envision that the availability of a large data network will then facilitate and coordinate basic and clinical CLL research in Australia.

Colorectal

Associate Professor Peter Gibbs is the BioGrid Colorectal cancer tumour stream leader. He is a joint Laboratory Head, Colorectal Cancer Biomarker Laboratory at the Ludwig Institute for Cancer Research (LICR) and Senior Staff Specialist at The Royal Melbourne and Western Hospitals.

Background

Colorectal cancer is the second most common cancer affecting men and women in Australia, and the second leading cause of cancer related death. Considerable progress has been made in treating patients with advanced disease, but a greater focus on understanding outcomes for individual patients and optimising treatment selection will further improve outcomes. Improving the quality of care is vital, with a focus on ensuring that every patient has optimal initial assessment, therapy and follow-up. Ultimately earlier diagnosis of disease through developing new screening tools and optimising use of existing technology will have the biggest impact on the number of cases and Colorectal cancer related mortality.

Progress and Challenges

Sites

This year has seen an expansion of the number of sites collecting Colorectal cancer data and the range of research activities enabled by this collection. Every public hospital in Victoria where there are specialist colorectal surgeons operating is now collecting data using the BioGrid and CSSANZ defined dataset and the BioGrid ACCORD database. Increasing involvement of the private sector is also being seen, with data now being captured at five private hospitals. Major projects that these sites are contributing to include the ongoing Victorian Cancer Agency supported tumour stream work exploring prognostic and predictive markers in stage II and III Colon cancer, including tumour and patient related markers. Increasingly the ACCORD Colorectal cancer database is being used at interstate sites, with at least one site now collecting Colorectal cancer data in each site being South Australia, New South Wales, Australian Capital Territory and Tasmania.

Research

Highlights have included the publication of papers combining BioGrid linked data with Victorian Cancer Biobank provided tissue based research (publication references 4,6), and a series on lymph node yield in Colorectal cancer (3) that included over 10,000 cases and demonstrated that large datasets can be generated and used through BioGrid. Other significant papers reported on the value of data linkage with the Victorian Cancer Registry (1) and the limited knowledge that clinicians have of their own clinical practice (9), which highlighted the importance of prospective data collection in defining and understanding what is happening in routine care. Importantly these publications included the first combined analysis with an international partner (6), in a combined study with researchers at MD Anderson Cancer Center. Other papers related to better understanding outcomes in routine clinical care (7,8) and how to optimise these, using BioGrid linked data to explore treatment selection (5) quality (2) and safety issues. New areas of research include detailed analysis of the cost of treating Colorectal cancer (paper submitted) and demonstrating the cost-effectiveness of FOBT screening (paper submitted). The first reports related to a Roche sponsored, prospective, multi-centre project collecting data on patients with newly diagnosed metastatic Colorectal cancer were generated, with data on 250 patients now having been entered.

[1] Source: Leukaemia Foundation website: www.leukaemia.org.au

It is anticipated that this 1,000 patient study will finish accruing mid 2012. Multiple data collection projects in partnership with industry are being explored, with the focus on adding value to BioGrid and facilitating research, and ensuring that the principles of BioGrid are not compromised.

Grants

Major success was achieved with four applications where BioGrid was the basis of data collection for translational research projects receiving funding during 2010. These related to exploring the role of circulating tumour DNA as a marker of outcome in patients with Colorectal cancer and Liver metastases (funded by LICR) and patients with stage II Colon cancer (funded by Victorian Cancer Agency). A LICR project funded by an NHMRC project grant will explore a range of tissue biomarkers. An NHMRC development grant exploring novel biomarkers as a diagnostic panel for Colorectal cancer included BioGrid as the mechanism for data collection and linkage. These projects combined are contributing significant revenue to BioGrid and are demonstrating the value that BioGrid enabled data collection and linkage can bring to a broad range of research projects.

Future Directions

Increasing the number of sites collecting Colorectal cancer data, with a particular aim on increased engagement from medical oncologists will be a focus for the coming 12 months. This will be enabled by grant and industry funded projects that provide vital support for data collection and initial establishment of BioGrid infrastructure at each site, supporting sites to initially engage with BioGrid and to continue to collect data.

To ensure the sustainability of data collection and BioGrid enabled research, there will be a continued focus on integrating data collection into routine care, with the electronic chemotherapy prescribing tool (which generates prescriptions and collects data) about to be rolled out at multiple sites. The value of this is enhanced by linkage with EviQ, providing clinicians with up to date protocols and treatment information. Also being considered are similar projects (generating data required for routine care and capturing data concurrently) related to operating reports, pathology reports, discharge summaries, and outpatient notes.

Publications

1. Field K, Kosmider S, Johns J, Gibson K, Farrugia H, Jones IT, McLaughlin S, Chapman M, Harold M, Murigu G, Gibbs P. Linking Data from Hospital and Cancer Registry Databases. Should this be Standard Practice? *IMJ* 40;566-573:2010
2. Kosmider S, Shedda S, Jones IT, Gibbs P. Predictors of clinic non-attendance - opportunities to improve patient outcomes in colorectal cancer *IMJ* 40;757-763:2010
3. Field K, Platell C, Rieger N, Skinner I, Wattchow D, Jones I, Chen F, Kosmider S, Wohlers T, Hibbert M, Gibbs P. Lymph node yield following colorectal cancer surgery in Australia. *ANZJS*. Accepted April 2010
4. Tie J, Gibbs P, Lipton L, Jorissen R, Burgess AW, Croxford M, Jones I, Langland R, Kosmider S, McKay D, Bollag G, Nolop K, Sieber OM, Desai J. Optimizing Targeted Therapeutic Development: Enriching the Colorectal Cancer Patient Population for the $BRAF^{V600E}$ Mutation. *Int J Cancer*. Accepted June 2010
5. Ananda S, Kosmider S, Lim L, Barnett F, Desai J, Gibbs P. Adjuvant Chemotherapy For Stage II And Stage III Colon Cancer – What Is Happening In Routine Practice In Australia? *JOP* Accepted April 2010
6. Tran B, Kopetz S, Tie J, Gibbs P, Jiang Z, Lieu C, Agarwal A, Maru D, Sieber O, Desai J. Impact of BRAF Mutation and Microsatellite Instability on the Pattern of Metastatic Spread and Prognosis in Metastatic Colorectal Cancer. *Cancer*. Accepted December 2010
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Gynaecology

Dr Sumitra Ananda is the BioGrid Gynaecological tumour stream leader. She is a Medical Oncologist at The Royal Women's Hospital and Western Hospital.

Background

Gynaecological cancers include cancers of the uterus (including endometrium), ovary, cervix, vulva, vagina, and placenta and gestational trophoblastic disease (pregnancy-related cancers). On average, more than 3,900 women were diagnosed with a gynaecological cancer in Australia each year, between 2001 and 2005. Gynaecological cancers were responsible for 1,562 female deaths in Australia in 2005, accounting for 9.1% of all female cancer deaths.

Progress

The Ministerial Taskforce for Cancer (2003-2007), established by the Victorian Government provided seed funding in 2005 to initiate the Victorian Cancer Outcomes Network (VCON) project. A pre-trial commenced in June 2006 with the capture and transfer of Victorian Clinical Cancer Registration Dataset (VCCRD) data from the Oncology Unit at The Royal Women's Hospital to the Victorian Cancer Registry. The Royal Women's Hospital collect data using a database known as GeMMA. The success of the pre-trial led the Cancer Council Victoria to fund a one-year project know as the Gynaecological Oncology Project (GOP). This project commenced in 2008 to expand Gynaecological data collection to the other major metropolitan and regional Gynaecological treatment centres using the GeMMA software. This enabled the Victorian Cancer Registry to expand the existing data collection to include clinical data based on the VCCRD and report on surveillance and monitoring for Gynaecological tumour stream at the population level for Victoria. The project promoted and expanded Gynaecological cancer data collection at several metropolitan health services using the GeMMA software.

Currently, BioGrid is in the process of linking with The Royal Women's Hospital, which is the largest provider of Gynaecological oncology care in Victoria. The GeMMA database has been used for clinical research and in particular two abstracts and papers have been submitted and presented at international Gynaecological cancer meetings.

Future Directions

To further establish the Gynaecological Tumour Stream as part of the current BioGrid tumour streams will be the ongoing focus. The Gynecological Oncology Project (GOP) demonstrated a need to collect clinical information for Gynaecological cancers. BioGrid is making links with other sites in Victoria to enable the utilisation of their comprehensive data for translational research purposes and linkage analysis.

Presentations

Ananda S, Gibbs P, McNally O, Quinn M. Factors associated with enrolment in Ovarian Cancer Clinical Trials and the impact on outcome. Oral presentation at International Society of Gynaecological Oncology. Prague October 2010.

Head and Neck

Mr David Wiesenfeld is the BioGrid Head and Neck tumour stream leader and Clinical Associate Professor at The University of Melbourne. He is an Oral and Maxillofacial Surgeon at The Royal Melbourne Hospital with research affiliations at The University of Melbourne.

Background

The management of patients with Head and Neck tumours involves specialised, multidisciplinary medical care and input from sub-specialised allied health members including Otorhinolaryngologist Head and Neck, Oral and Maxillofacial and Reconstructive Plastic and Endocrine Surgeons, Medical and Radiation Oncologists, Radiologists, Pathologists, Dentists, Endocrinologists, Speech Pathologists, Nutritionists, Prosthetists and Nurses. Thyroid cancer is included in this tumour stream.

Progress and Challenges

The Head and Neck module in ACCORD is now in its fourth year of use. It has been invaluable for clinical research into Head and Neck cancer at The Royal Melbourne Hospital. The appointment of Charlotte Crill as Head and Neck Database Manager has ensured the completeness and accuracy of data entry for patients. The inclusion of Radiation and Medical Oncology data remains a priority. The development of The Victorian Comprehensive Cancer Centre should allow us to fulfil this goal.

A proud achievement for the year was being presented with the Melbourne Health "Best of Health" award to The Thyroid Cancer MDT enthusiastically led by Dr Julie Miller. The Thyroid cancer MDT continues to strengthen its clinical role. It is hoped that sufficient funds will be found this year to create a specific ACCORD Thyroid Database.

Projects completed and either accepted or submitted for publication include:

1. A review of 71 patients with oral tongue cancer for the impact of close and positive margins on outcome. (Submitted for publication Head and Neck Journal).
2. A review of quality of life improvement for 29 patients having dental implants after treatment for oral cancer. (Accepted for publication Australian Dental Journal).
3. A review of the efficacy of pre-operative chemotherapy for 15 patients with osteosarcoma of the facial bones, comparing the extent of tumour necrosis with disease control. (Accepted for publication Journal of Oral and Maxillofacial Surgery).
4. A review of clinical outcomes for 24 patients with adenoid-cystic carcinoma of the minor salivary glands. (Accepted for publication International Journal of Oral and Maxillofacial Surgery).
5. A review of regional failures of patients with oral tongue cancer with and without neck dissection by depth of tumour. (Accepted for publication Otolaryngology, Head & Neck Surgery Journal).

Projects currently in progress include:

1. Analysis of patients with oral cancer, comparing the demographics and outcomes for those who are non-smokers, and non-alcohol drinkers, with those who have consumed significant amounts of tobacco and alcohol. This project has attracted the generous support of a grant from the Price Family Foundation.
2. Prospective correlation of radiological, clinical, and pathological assessments of tumour thickness in the anterior tongue. This project has nearly completed the accrual phase, and is expected to be published by the end of 2011.
3. Analysis of outcomes for patients managed with mid-facial cancer.

All of these projects rely on accurate data within our ACCORD Database. The contributions of researchers, Tim Iseli, Michael McCullough, Arun Chandu, Pramit Phal, Catherine Spinou, Adrian De Angelis, Mathew Linn, Roland Barrowman, Kendrick Koo, and Alex Bobinskas are gratefully acknowledged.

Future Directions

The challenge of spreading the use of the ACCORD Head and Neck database to additional sites is significant and requires ongoing effort. The development of the database for MDT presentations, referrer communications, and as part of the patient clinical record, is an area that demands financial and intellectual support.

Hepatocellular Carcinoma

Associate Professor Amanda Nicoll is the BioGrid Hepatocellular Carcinoma (HCC) tumour stream leader. She is Head of Hepatology at The Royal Melbourne Hospital.

Background

Worldwide, HCC is the fifth most common cancer and the third most common cause of cancer-related death. HCC is by far the most common primary liver cancer, being responsible for 75–90% of liver cancers worldwide. While HCC remains relatively uncommon in Australia, incidence rates have been progressively rising over the last few decades, due to increased cases attributed to hepatitis C and from hepatitis B – the latter related to migration from high prevalence countries. Adding to this is the obesity epidemic and increased cirrhosis due to non-alcoholic steatohepatitis (NASH, Fatty liver disease).

HCC has well-defined risk factors, some of them amenable to modulation or eradication. The treatment of HCC is increasingly multidisciplinary and outcomes continue to improve due to advances in percutaneous therapies such as chemo-embolisation and radiofrequency and microwave ablation. While HCC responds poorly to conventional chemotherapy, biological agents that specifically target the molecular basis of neoplastic growth and metastasis are expected to make a significant impact on outcomes in coming years. Vascular endothelial growth factor inhibitors have been shown to improve survival in randomised controlled trials.

Therapy, outcomes and prognosis in HCC are intimately linked to both tumour characteristics and organ (liver) function. The lack of appropriate staging systems that recognise the unique nature of HCCs has been a significant impediment to establishing standardised treatments. The Barcelona Clinic Liver Cancer staging system that captures the required details, has been widely endorsed and is increasingly used for guiding patient management and assisting patient selection into clinical trials which will add to standardisation in the future. Including this staging data along with the collection of details related to treatments used and outcomes achieved in routine practice will substantially inform optimal treatment selection and lead to improved outcomes.

Progress and Challenges

The Melbourne HCC Interest Group (HCCIG) was established in 2010 as an offshoot of the Melbourne Liver Group (MLG), and includes representatives from each of the seven main Melbourne hospitals. In addition to hepatologists, it now involves clinicians from across all specialty groups involved in the management of HCC. One issue highlighted was the paucity of linked local data on the epidemiology, management patterns and outcomes of these patients in the light of new interventional and systemic therapies. Also discussed was the lack of a standardised approach to the management of these patients. HCCIG outlined that collaboration was needed to form a HCC Registry in Victoria to evaluate and assess the diagnosis, epidemiology and treatment of HCC in Victoria and in the future in Australia.

HCCIG is currently working with BioGrid to develop a generic HCC ACCORD module to enable data collection across seven patient treatment sites in Victoria namely; Austin Hospital, Box Hill Hospital, Monash Medical Centre, St Vincent's Hospital, The Alfred, The Royal Melbourne Hospital and Western Hospital.

Future Directions

The ACCORD HCC database, once implemented at patient treatment sites across Victoria, will establish the IT infrastructure to collect HCC data in a uniform manner that could be installed across all HCC treatment centres in Australia. This would mean that HCC researchers would have access across geographic regions and health organisations to thousands of patient treatment records, enabling:

- Higher confidence levels in research outcomes;
- Ability to track best practices across HCC treatment sites; and
- More effective human and funding allocation as less will be spent on data collection and more on analysis.

Lung

Dr Matthew Conron is the BioGrid Lung tumour stream leader and Respiratory Physician at St Vincent's Hospital.

Background

There is increasing recognition that the poor outcomes for patients with Lung cancer are in part linked to the absence of comprehensive research programs into this lethal tumour. Close to 2,000 Victorians die each year from Lung cancer, more than from Colon and Breast cancer combined. This deficiency in cancer research is slowly changing with a number of recent advances that have identified small groups of patients who will benefit from targeted therapies, in particular the Epidermal Growth Factor Receptor (EGFR) and Anaplastic Lymphoma Kinase (ALK) inhibitors. While these advances are encouraging, more work is required to identify novel therapies for the majority of patients who do not yet have effective treatment. BioGrid is playing a critical role in helping to translate advances in basic science research to the management of patients with Lung cancer, by helping to define clinical phenotypes through the collection of comprehensive clinical datasets.

Progress and Challenges

Lung cancer care is diffused across multiple medical disciplines and throughout the private and public hospital system. This poses unique challenges for data collection and research, because there is no consolidation of care at one site within Victoria. In an effort to overcome some of the limitations in state wide data collection a registry is being developed as part of a Victorian Cancer Agency (VCA) funded initiative, using a consensus minimum dataset that was developed by BioGrid in collaboration with the Victorian Cooperative Oncology Group Lung Group and Integrated Cancer Services. The VCA funding will support construction and installation of a Lung cancer database (adding to the BioGrid suite of ACCORD databases), provide support to assist with data collection, and facilitate translational research across all of the major Melbourne centres involved in the treatment of Lung cancer. Additional objectives include documenting variations in care and tracking outcomes in patients across Victoria. BioGrid's capacity to link common datasets is ideally suited to this task.

Future Directions

It is anticipated that BioGrid will play a critical role in maximising the value of the data collected on the treatment and outcomes of patients with Lung cancer, and will facilitate collaborative research across multiple centres. Research combining tissue and data to study biomarkers in this disease and to assist with the discovery and development of new therapies will be enabled.

Melanoma

Associate Professor Grant McArthur is the BioGrid Melanoma tumour stream leader. He is a Medical Oncologist and Head of the Molecular Oncology and Translational Research Laboratories at Peter MacCallum Cancer Centre.

Background

Melanoma is the most serious type of skin cancer, and the third most frequently occurring form of cancer in Australia. Melanoma has become a serious Public Health threat, with incidence rates currently increasing faster than for any other cancer.

The latest statistics from the Cancer Council of Australia show that Australia has one of the highest rates of Melanoma in the world. Each year, over 10,300 Australians are diagnosed with Melanoma, and research published by the Cancer Council Australia estimates Melanoma treatment costs the health system $300 million each year, with young people being at particular risk; Melanoma accounts for the loss of more productive years of life than any other type of cancer.

Progress and Challenges

The Melbourne Melanoma Project (MMP) is leading programs in Melanoma research across Victoria to improve diagnosis and early detection, gain more accurate tools to predict outcome and target new Melanoma therapies for the patients at most risk. Peter MacCallum Cancer Centre, Victorian Melanoma Service - Alfred Hospital and the Austin Hospital, are the initial sites comprising the Melbourne Melanoma Project.

MMP mutually agreed standard Melanoma clinical datasets have been defined and data collection is well underway with collaborators able to access clinical information and matched paraffin embedded tissue on over 400 clinical cases. This has offered unique opportunities to study the underlying molecular and genetic changes in a large caseload of Melanomas where full clinical information is also available.

MMP is now working with the Victorian Cooperative Oncology Group Melanoma Group and Integrated Cancer Services to develop a Skin Cancer and Melanoma Victorian wide Consensus Dataset. Standard datasets will be included in the BioGrid suite, with a plan to use BioGrid to link data across sites.

The attainment of a Victorian Cancer Agency (VCA) Translational Research Grant has enabled the commencement of additional collaborative research to establish and link leading programs in Melanoma research across Victoria to improve diagnosis and early detection, gain more accurate tools to predict outcome and target new Melanoma therapies for patients at most risk.

The last year's highlights for the Melanoma tumour stream are:

- Successful attainment of VCA translational research grant to the value of $3.27 million.
- Preliminary recommendations for the establishment of a national collaborative engagement strategy for the early detection and management of Melanoma.
- Presentation of findings at the American Society of Clinical Oncology conference.
- Recruitment of Dr Mark Shackleton and Dr Tom John to continue ground breaking research in human Melanoma biology.
- The implementation of an integrated web based database across sites continues to be a challenge.

Future Directions

During the next 12 months the group will continue to expand on ongoing research projects supported through the VCA translational research grant. A Consumer Reference group has been established and this group will work towards raising community awareness of our research activities in order to gain an improved understanding of the diagnosis and management of Melanoma and establish a premier forum for dissemination of outcomes the research has undertaken. We will also continue working with the Skin Cancer and Melanoma Consensus Dataset Working Group in order to finalise a state-wide Melanoma dataset.

Pituitary

Associate Professor David Torpy is the BioGrid Pituitary tumour stream leader and a Consultant Endocrinologist at the Royal Adelaide Hospital.

Pituitary disease accounts for a diverse range of clinical syndromes resulting from the role of the pituitary as the 'master gland' regulating the function of many other endocrine glands and its proximity to other important intracranial structures, particularly those that affect vision. Tumours, which are most often benign, are frequent causes of Pituitary disease and the management options involve surgery, medication to alter tumour biology and hormone secretion and radiotherapy.

Background

There is a need to better understand the natural history of patients with Pituitary disease as well as evaluate the effectiveness of Pituitary therapies in an Australian context. It is hoped such a database will be useful for audit/quality control purposes and also for research purposes.

Using the resources of BioGrid, three Australian hospitals are developing databases of patients treated over the past 10-15 years with an ongoing commitment to add prospective data to the database. It is hoped other hospitals will join in this initiative.

Progress and Achievements

The Royal Adelaide Hospital has produced a data collection instrument in collaboration with several other Australian centres. We have complete data on approximately 600 patients treated over 20 years. The Royal Melbourne Hospital and Vellore Hospital in India have added data from 200 and 150 patients, respectively. The plan is to involve more hospitals, several of whom have expressed interest to obtain a complete picture of Pituitary disease management in Australia and with an international comparator in India. A recent analysis of the prognosis of patients with cavernous sinus invasion by tumour, a generally inoperable region, has been completed by Ms Georgina Irish, medical student at the University of Adelaide, and a manuscript is in preparation.

Challenges and Future Directions

The main challenge for the coming year is the continued collaboration with hospitals in Australia. Currently, a number of data analyses are in progress which is likely to lead to publications and assist with efforts to obtain longer term funding.

Rare Tumours

Associate Professor Clare Scott is the leader of the BioGrid Rare Tumour stream. She is a Medical Oncologist at The Royal Melbourne Hospital and The Royal Women's Hospital and a Laboratory Head at the Walter and Eliza Hall Institute of Medical Research.

Background

The Rare Tumour stream encompasses over 500 malignancies and also includes rare subsets of common tumours. Although particular tumour types occur rarely, when all the different kinds of 'Rare Tumours' are taken together they make up 20% of all cancers diagnosed.

Progress and Challenges

The primary focus of the Rare Tumour stream continues to be the development of the online database known as CART-WHEEL, the Centre for Analysis of Rare Tumours. CART-WHEEL.org was launched in April 2010 by Professor Sir Gustav Nossal. The generation of this web-based Rare Tumour Database, utilising the BioGrid Australia infrastructure, is the first ethically-approved portal for consumer–driven information collection for Rare Tumours. The website has been developed with significant consumer input, particularly from Cynthia Pollack (HEARD Database) and John Stubbs (Cancer Voices Australia) to ensure that it is accessible, user-friendly and relevant to consumers. Information, including a brochure, is available from www.CART-WHEEL.org. Patients or their proxies can log on and enter their data into the sophisticated, yet easy to use questionnaire and then download a PDF summary of their information for their use.

Dr Susie Bae a Clinical Research Fellow with BioGrid Australia and Ludwig Institute for Cancer Research, will commence in February 2011 to drive awareness of, and specific projects for, CART-WHEEL, funded by the Victorian Cancer Agency and The Picchi Brothers Foundation. This includes primary validation of the quality of consumer-entered data in CART-WHEEL.

The database is available for use by researchers wanting to identify larger groups of patients with a particular tumour type in order to conduct more meaningful research. It is hoped that it will also contribute substantially to identification of people who may be relevant for clinical trials of novel targeted therapeutics. The online format will allow identification of consumer participants on an international scale, with the individual's level of involvement in the project reflecting the level of consent they have provided. Researchers can apply to BioGrid for access to the data that is collected with the scientific validity and feasibility of their request assessed by a BioGrid committee.

Future Directions

Raising awareness of CART-WHEEL, including by harnessing social networking approaches is our focus for 2011. We have three specific projects, which will provide basic proof of concept for the utility of CART-WHEEL. A pilot study of the data contained within CART-WHEEL will be submitted to Melbourne Health HREC in the first half of 2011.

Renal

Associate Professor Ian Davis is the BioGrid Renal tumour stream leader and a Medical Oncologist and Cancer Immunologist. He has a clinical appointment at Austin Health and is currently an Associate Member of the Ludwig Institute for Cancer Research where he is also Head of the Uro-oncology laboratory.

Background

Renal cancer is the ninth most common cancer in Australia and the fifteenth most common cause of cancer death[1].

Progress and Challenges

The dataset developed by Austin Health and The Royal Melbourne Hospital is now established and fully operational at Austin Health. Data entry is web based and the forms are simple and intuitive. The database was developed to be used in clinics so has functionality that directs the user to complete appropriate screens, highlights incomplete pages and minimises the number of mouse clicks by using radio buttons where appropriate.

Funding from the Victorian Cancer Agency contributed to the database development and has funded a project manager to facilitate data and tissue collection at Austin Health in conjunction with the Ludwig Institute for Cancer Research, the Victorian Cancer Biobank and BioGrid. Progress in this tumour stream was presented at the Victorian Cancer Agency on 17 August 2010.

Future Directions

The functionality of the database is currently being reviewed to improve its value to clinicians. In particular, aspects relating to collection of surgical audit data are being addressed and will probably result in further modifications to the database in the near future. This will optimise data entry by specialties other than medical oncology. The database is planned to be rolled out to other BioGrid member sites. Cancer Trials Australia forums and Clinical Oncology Society of Australia meetings will also be used to promote the system.

Future research includes tissue analysis with associated clinical data. Specific projects related to information required by external providers such as industry are also under consideration.

The development of research projects in collaboration with industry is well underway. A specific project funded by Pfizer will initially examine retrospective data on 200 patients with advanced Renal cancer treated across four BioGrid member sites. A prospective project will then commence, with many more sites planned to be involved.

[1] Cancer in Australia: an overview, 2010. At http://www.aihw.gov.au/publications/can/56/12138.pdf

Research Reports: Life Sciences

Cystic Fibrosis

Professor John Wilson is the BioGrid Cystic Fibrosis (CF) disease stream leader. He is head of The Cystic Fibrosis service at the Department of Allergy, Immunology and Respiratory Medicine at The Alfred Hospital and on the Faculty Board of Monash University Medical School. In addition to the Alfred Hospital, the BioGrid CF stream includes Monash Medical Centre under Associate Professor David Armstrong and The Royal Children's Hospital (RCH) under Associate Professor Philip Robinson.

Cystic Fibrosis is a devastating disease for which there is currently no cure. It affects the mucous glands of the lungs, liver, pancreas, and bowel, causing progressive disability due to multisystem failure and eventual death. However the introduction of aggressive treatment regimes has seen patient survival improve from an average of 20 to 30 years a generation ago, to the point where many patients are now surviving into their 40's and beyond.

Progress and Achievements

The main aim of the BioGrid CF group was to connect the lung function databases from the three participating sites to the BioGrid system. All three centres treating CF in Victoria are connected and this has allowed a state-wide population of patient information to be available for research. It allows tracking of patient information (in de-identified form) from childhood treatment through to treatment as an adult.

The past year has seen the analysis of Lung Function data from all the three hospitals through the BioGrid system. In addition, data from RCH covering treatment over the last 25 years has provided a rich source which is being examined for treatment trends and outcomes over time. Information includes patient admission, length of stay and co-morbidities. The impact of the introduction of newborn screening was also examined.

Challenges and Future Directions

Current work on obtaining data from the Smarthealth system was delayed but will occur in 2011. Smarthealth is a full clinical system for CF patients that is being installed over time at the three participating hospitals, and will contain full clinical details and patient management notes. When linked to the admissions and lung function data, it will provide a valuable resource for the study of CF. A paper was presented to the Australian CF Society meeting in September 2009 showing the improvements in patient survival over the past 10 years, and a paper modelling disease outcome is expected to be presented at Australian and USA CF conferences in 2011.

Diabetes

Professor Peter Colman is the BioGrid Diabetes disease stream leader. He is Head of Department of Diabetes and Endocrinology at The Royal Melbourne Hospital and Division Head of Structural Biology at The Walter and Eliza Hall Institute of Medical Research.

Background

Diabetes is a major health priority for the community with the incidence of both Type 1 and 2 Diabetes increasing at an alarming rate. This chronic disease affects 4% of the Australian population. Type 2 Diabetes represents 85-90% of all cases of Diabetes and the remaining 10-15% accounts for Type 1 Diabetes mainly affecting children and adolescents. Treatment for both types of Diabetes can be complex and there is a risk of complications affecting the heart, kidneys, eyes and nerves.

Progress and Challenges

The Diabetes stream consists of two areas – Clinical Diabetes and Preclinical Type 1 Diabetes research. The Clinical Diabetes area is the most active with clinical data from The Royal Melbourne Hospital, The Royal Children's Hospital, Austin Hospital and St Vincent's Hospital continuing to accrue. The major focus of research is clinical outcomes of Diabetes with emphasis on approaches to improve outcomes. The Type 1 Diabetes research area is extremely active, but during this period there has been limited use of this dataset.

Over the past year The Royal Melbourne Hospital data has been used extensively to evaluate Diabetes outcomes (through electronic submission of data to the Australian National Diabetes Information Audit and Benchmarking). This is the first time this has been achieved electronically and the programming for this is being applied to running of a continuing QA process for clinic outcomes.

Two researchers are now using combined Diabetes data from contributing hospitals to evaluate different aspects of Diabetes care and outcomes – retinopathy, nephropathy, peripheral vascular disease, peripheral neuropathy and cardiovascular outcomes. This is an exciting development. The data has also been used to identify people with Diabetes and specific characteristics to be involved in a number of clinical trials. Our major challenge is to continue to recruit researchers to work with our data and to make the interface with the data as friendly as possible.

Future Directions

There are a number of other research ideas which need further development and then funding. We need to involve more hospitals. Discussions have been had with Royal Adelaide Hospital and several other centres. Linking the data with State Government hospital outcomes data and death index remains a high priority.

Epilepsy

Professor Terence O'Brien is the BioGrid Epilepsy disease stream leader. He has appointments at the Department of Medicine and Department of Neurology, The Royal Melbourne Hospital and at The University of Melbourne.

Background

Epilepsy is the most common serious neurological condition worldwide. Between 5 and 10% of individuals experience a seizure during their life and 2 to 5% will develop Epilepsy, defined as more than one unprovoked seizure. Mortality among those with severe Epilepsy is two to three times greater than that of the general population. People with Epilepsy often have one or more co-morbidities and exhibit a two to five times greater prevalence of cerebrovascular and cardiovascular disorders, gastro-intestinal disorders, pulmonary disorders, and dementia across all age groups. Psychiatric disorders are amongst the more common co-morbidities. Depression is three to ten times more frequent in those with uncontrolled Epilepsy than the general population, and the overall suicide rate is five times higher. Falls, drowning, choking and burns comprise the most common causes of injury for people with Epilepsy. The outcomes of treatment for Epilepsy are often unsatisfactory, and unpredictable in an individual. At least 50% of patients will not have seizures control after starting a medication for Epilepsy, and at least 30% will never achieve seizure control despite trying multiple different medications. Adverse drug reactions occur in 30-40% of patients with each anti-epileptic drug tried. If women become pregnant while taking an anti-epileptic medication there is at least two to three fold increased risk of a foetal malformation, neurocognitive deficit or autism spectrum disorder.

Progress, Challenges and Future Directions

The research being facilitated by BioGrid is aimed at identifying predictors of adverse outcomes of Epilepsy and it's treatment which can be subsequently applied in clinical practice to improve certainty and quality of life for suffers of this common serious condition.

The following projects are currently being undertaken:

1. *Identification of pharmacogenomic predictors of treatment outcomes in Epilepsy*: We have obtained and published proof of concept data for the application of supervised learning approaches to develop a multigenic classifier for treatment outcomes in a cohort of 179 prospectively followed newly treated Epilepsy patients (Petrovski et al., 2009). This cohort has now been expanded to 450 Australian patients, and is being linked to 1,200 newly treated patients from the UK. These patients are having genome wide genotyping for >500,000 SNPs.
2. *The outcomes of patients newly presenting with a possible seizure disorder:* This project is linking the hospital based clinical, imaging and electrophysiology data from a cohort of 3,500 patients who have been seen in First Seizure Clinics over more than a decade with comprehensive government databases to provide internationally unique comprehensive data about Epilepsy, medical, psychiatric, injury, mortality and fertility data.
3. *KONQUEST study of outcomes of first substitution anti-epileptic drug therapy:* This world first study has randomised patients who have failed the first anti-epileptic drug, because of ongoing seizures or adverse drug reactions, to a new (leviteracetam) vs. older (carbamazepine or valproate) drug. A broad range of Epilepsy, side-effects, psychiatric, neurocognitive and quality of life outcomes are assessed. The study has now finished collecting data and is being written up for publication.

Publications

1. Petrovski S, Szoeke CEI, Jones NC, Salzberg MR, Sheffield LJ, Huggins RM, O'Brien TJ. Pre-Treatment Patient-Perceived Neurocognitive Symptomatology Predicts Seizure Recurrence in Newly Treated Patients. Neurology (In Press, accepted May 2010). [I.F. 8.172]

   This study shows that to develop the most accurate predictive models for treatment outcomes, multiple sources of information should be integrated, including historical, neuropsychiatric and genomic data. This will be very important in informing the design of future pharmacogenomic studies for Epilepsy and other complex diseases.

2. Jones SG, O'Brien TJ, Adams SJ, Mocellin R, Kilpatrick CJ, Yerra R, Lloyd JH, Velakoulis D. Clinical characteristics and outcome in patients with psychogenic non-epileptic seizures. Psychosomatic Medicine 2010;72:487-97. [I.F. 4.236]

   One of the largest published series of patients with video-EEG confirmed psychogenic non-epileptic seizures (PNES) with detailed neuropsychiatric assessments. Demonstrated that these patients experienced long delays in diagnosis and high rates (>80%) of prolonged, inappropriate, treatment with anti-epileptic drugs. Patients assessed at follow-up exhibited poor long-term outcomes with ongoing PNES, high rates of psychopathology, low rates of specialist follow-up, poor quality of life and poor overall levels of functioning. These results demonstrate the need for earlier diagnosis of PNES and co-morbidities, and highlight the need for diagnostic and therapeutic approaches which combine neurological and psychiatric perspectives.

3. Kwan P, Li HM, Al-Jufairi E, Abdulla R, Gonzales M, Kaye AH, Szoeke C, Ng HK, Wong KS, O'Brien TJ. Association between temporal lobe P-glycoprotein expression and seizure recurrence after surgery for pharmacoresistant temporal lobe Epilepsy. Neurobiology of Disease 2010;39:192–197. [I.F. 4.859]

   Identified a novel biomarker of patients who have recurrent seizures following Epilepsy surgery. If confirmed with subsequent replication studies, this could be used to optimally select patients for surgery and counsel patients about their likely outcomes.

Human Variome Project

Professor Richard Cotton is the BioGrid Human Variome disease stream leader. He is the Director, Genomic Disorders Research Centre and Convenor, Human Variome Project.

Background

This visionary project aims to collect all variants in all genes across the human genome, and annotate the variants with all information that assists in the interpretation of the DNA change with respect to human health and disease. This will be done globally via a network of Country Nodes. These Nodes are critical to ensure the flow of data for use by healthcare professionals and clinicians in diagnosing and treating their patients. Over the past year the Human Variome Projects (HVP) international activities have attracted a high level of interest and support with major contributions being made by China as well as HVP Nodes being formed in other countries including Malaysia, Kuwait, Greece, Korea, Egypt and Belgium. It is considered that assimilation of knowledge through the Human Variome Project is essential if humanity is to reap the rewards of the power of next gene sequencing. A lead example of the process and benefits of this vision is the International Society for Gastrointestinal Hereditary Tumours (InSiGHT) mismatch repair database, now curated from Melbourne.

Progress and Challenges

Important funding has been provided through a National eResearch Architecture (NeATS) Federal Government grant ($0.5M) and the establishment of the systems to collect data from Australian Laboratories is now well advanced. The Australian Node of the HVP website and the access to this data is expected to be launched on the 1st of April 2011. In the first instance, the Australian Node is concentrating on mutations in the MMR and BRCA genes and in Huntington's Disease. This work is being done by Alan Lo at the Victorian Partnership for Advanced Computing (VPAC) and is likely in the future to utilise BioGrid to connect to relevant clinical data, particularly given the wide acceptance that the BioGrid processes have earned from HRECs across south eastern Australia. Laboratories in Queensland, Victoria, New South Wales and South Australia will be initially supplying data to the Node.

Future Directions

The work will be extended to other DNA laboratories across Australia, and other genes. Linkages to a range of international Locus Specific Databases (LSDBs) are being planned, as is the passage of selected data to the National Centers for Biotechnology Information (NCBI) and the EU Bioinformatics databases.

Inflammatory Bowel Disease

Professor Finlay Macrae is the BioGrid Inflamatory Bowel Disease/Crohn's Disease stream leader. He is Department Head of Colorectal Medicine and Genetics and a Gastroenterologist at The Royal Melbourne Hospital.

Background

Inflammatory Bowel Disease (IBD) is a chronic inflammatory disease of the gastrointestinal tract, comprising two major subtypes – ulcerative colitis and Crohn's Disease. The condition is common, with the cause uncertain, but it is thought to represent a disordered immune response, perhaps genetically determined, to an environmental stimulus. The microbiota of the gut is under close scrutiny at present for its role in association with the host immune response. Most therapies are targeted at controlling the immune response, with expensive biological agents now emerging as the most effective therapies.

Melbourne IBD is the professional association of "IBDologists" who share their expertise at research and educational meetings. An IBD database has been developed at St Vincent's Hospital and adopted by Melbourne IBD as their preferred database. The database is installed at St Vincent's Hospital, The Royal Melbourne Hospital (RMH), Monash Medical Centre and The Alfred.

Progress and Challenges

At RMH we continue to collect data, though even with this task we struggle due to limited resource and an expanding clinical workload. On a positive note, we have managed to secure funding for a full time IBD clinical nurse specialist and we expect this will assist in the database management. Clinicians with IBD expertise are located at the following centres: RMH: Finlay Macrae, Bernadette Viney; St Vincent's: Sally Bell and Bill Connell; Monash Medical Centre: Greg Moore; Alfred Hospital: Simon Jacobovitz and Miles Sparrow; The Royal Children's Hospital: Tony Catto-Smith. Our aim in the future is to conduct research across the multiple centres involved.

Future Directions

In the future there is the potential to link to IBDologists in IBD Australia, a well established subspecialty group of the Gastroenterological Society of Australia.

Refugee Health

Associate Professor Beverley-Ann Biggs is the BioGrid Refugee Health disease stream leader. She is an Infectious Diseases Physician, Victorian Infectious Diseases Service (VIDS Clinic) at The Royal Melbourne Hospital and also has an appointment at The University of Melbourne working in International Health, Department of Medicine.

Background

Refugee health is an emerging specialised clinical area, with around 4,000 people of a refugee background settling in Victoria annually. Refugee patients require specific health screening for infectious diseases and nutritional deficiencies after they arrive in Australia; they typically have multiple complex health conditions and require medium to long-term follow-up. Clinical care is challenging, due to the number and complexity of their medical problems, the need for multiple screening tests and the fact most health care is delivered with the help of an interpreter. Victoria now uses a primary care model of refugee health screening; however available evidence suggests at least 50% of refugees require specialist referral. Both primary care providers and specialists must be aware of patients' results, management, medication and follow-up plans, requiring a clear flow of information to avoid duplications and improve outcomes. There are no systems currently in place that allows direct sharing of clinical information between hospitals and primary care, even though this is fundamental for coordinated care.

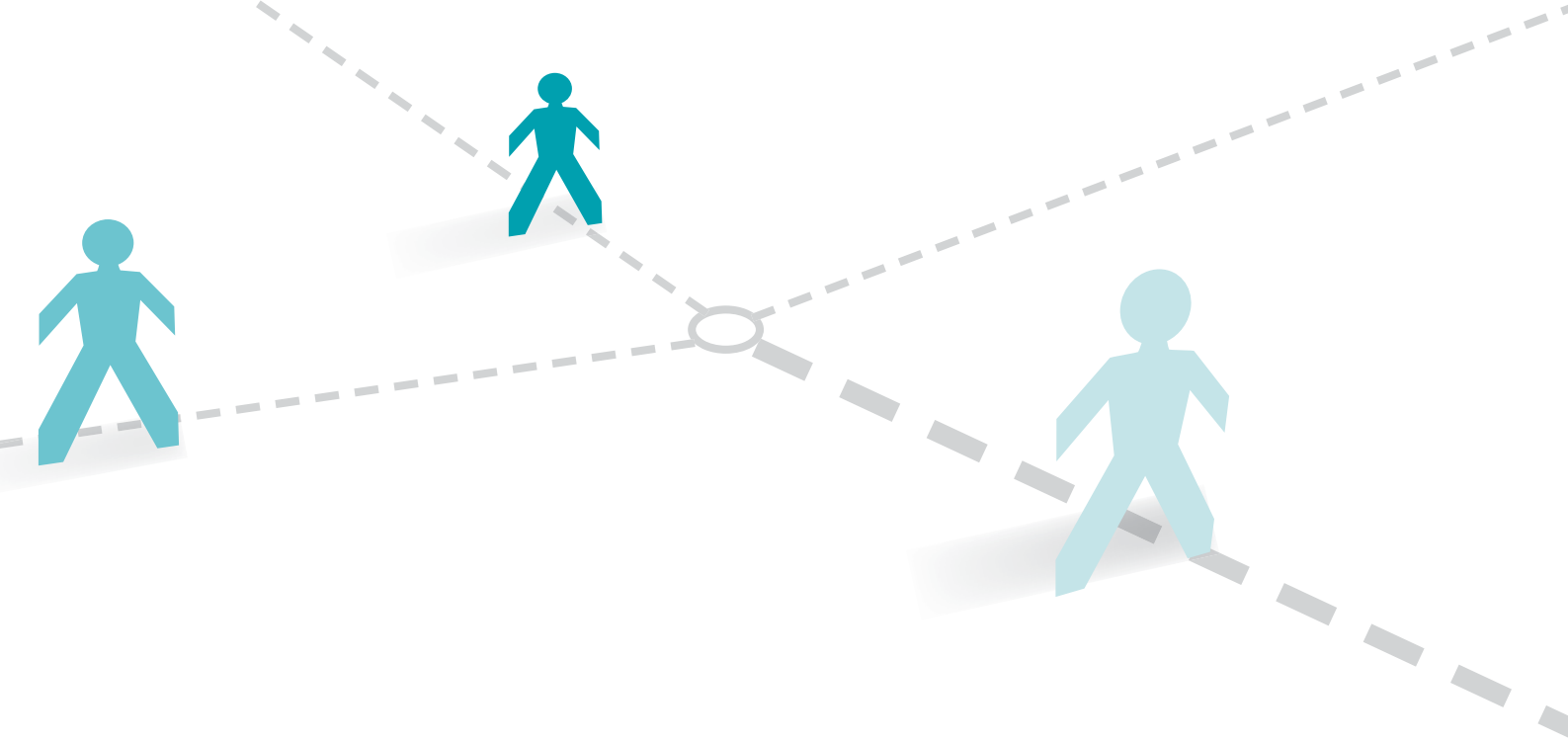
To date there has been extremely limited prospective data collection in refugee health, and no way of gathering population data across primary and specialist care, or collecting data on long term outcomes. Typically, by the time demographic information has been collated, the Humanitarian intake has changed, and the information is 'out of date'.

We are developing a web-based electronic health record for refugee patients across the four specialist adult and paediatric refugee clinics in Victoria. The system will utilise BioGrid to develop a platform for research in this group, allowing rapid epidemiological data collection and responsive evaluation of guidelines, practice and service delivery. Ultimately we hope this will form part of a web-based refugee health clinical hub, which will include a primary care/specialist interface, a patient held record/portal, and facilities for remote telehealth support for general practitioners.

Progress and Challenges

The project commenced in August 2010. Over the past six months we have:

- Reviewed the literature on computerised decision support systems.
- Mapped existing electronic clinical records/clinical databases.
- Consolidated a project working group including clinical (RMH and RCH specialists) and technical partners (BioGrid, Arcitecta, VPAC, Precedence healthcare (CDM-net), RMH IT department).
- Mapped workflow and clinician requirements in the specialist refugee clinics and developed a preliminary measure of service delivery to monitor implementation.
- Drafted the 'content' required for a web-based patient health record and point of care decision support tool and examined the integration with existing hospital systems.
- Applied for additional project funding.



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“I’m excited about the future of clinical research. I think so many things are bursting wide open, and when I look at the contribution being made by BioGrid, I get even more excited.”

Sir Gustav Nossal, Professor Emeritus, Department of Pathology, The University of Melbourne

BIOGRID
AUSTRALIA
Health through information

BioGrid Australia
ABN: 31 136 185 647

6 North, Main Building
The Royal Melbourne Hospital
300 Grattan Street
Parkville 3050
Victoria, Australia

T: +613 9342 3167
F: +613 9342 8548

enquiries@biogrid.org.au
www.biogrid.org.au