

**Boston Medical Center  
2011 Cancer Program  
Annual Report**

Multiple Myeloma and AL Amyloidosis  
with 2006-2010 Cancer Registry Data



**BOSTON  
MEDICAL**  
CENTER

EXCEPTIONAL CARE. WITHOUT EXCEPTION.



Dear Friends:

This cancer program annual report focuses on Boston Medical Center's activities in multiple myeloma and immunoglobulin light chain (AL) amyloidosis from 2006 through 2010.

The largest safety net hospital in New England and the primary teaching affiliate of the Boston University School of Medicine, Boston Medical Center is at the forefront of clinical practice, teaching and research in multiple myeloma and AL amyloidosis. At BMC, patients with these diseases receive state-of-the-art diagnosis and treatment by specialists who are renowned both as clinicians and researchers.

In our highly supportive and collaborative environment, experts in these diseases and related specialties provide patients with the most advanced, coordinated and comprehensive care available anywhere — treatment that is aggressive and innovative in controlling these diseases and managing their impact on our patients' quality of life.

An internationally recognized leader in the treatment of AL amyloidosis, the Autologous Stem Cell Transplant Program of Boston Medical Center collaborates with the Amyloid Treatment and Research Program at the Boston University School of Medicine, one of only a handful of major centers in the world dedicated to the study and treatment of AL amyloidosis. Together, we have pioneered treatment that improves survival and remission rates of patients with this deadly and rare disease.

Demonstrating the effectiveness of these breakthroughs, BMC achieved a five-year survival rate of patients with myeloma that is notably higher than the National Cancer Database (NCDB) outcomes, exceeding the nationwide rate by 11 percent.

In 2011, BMC accomplished another milestone as a cancer center: we received three-year re-accreditation by the American College of Surgeons Commission on Cancer as a Teaching Hospital Cancer Program, with commendation.

At BMC, our mission is to deliver exceptional care, without exception. We are proudly and passionately striving to improve outcomes for patients with multiple myeloma and AL amyloidosis.

Sincerely,

Vaishali Sanchorawala, MD  
*Editor, 2011 Cancer Program Annual Report;  
Clinical Director, Autologous Stem Cell  
Transplant Program; Boston Medical Center  
Professor of Medicine*

Lisa Kachnic, MD  
*Chair, Radiation Oncology; Chair, Cancer Care  
Committee; Boston Medical Center  
Professor of Radiation Oncology*

## Multiple Myeloma and AL Amyloidosis

Myeloma (also known as multiple myeloma or plasma cell myeloma) is the second most common blood cancer in the United States and constitutes about one percent of all cancers. Its overall incidence and mortality rates have remained fairly stable over the past two decades. In 2011, an estimated 20,520 American men and women will be diagnosed with myeloma and about 10,610 people will die of the disease. Based on rates from 2006 to 2008, 0.65 percent of men and women born today will be diagnosed with myeloma. However, recent data suggests that the incidence of myeloma and related diseases is increased 2.5 to 3-fold in African-Americans, making these diseases of even greater importance to BMC patients and doctors.

Multiple myeloma is the most common type of malignant plasma cell disorder, a disease characterized by clonal proliferation of immunoglobulin-secreting, differentiated B-lymphocytes and plasma cells. Other forms of malignant plasma cell dyscrasias include monoclonal gammopathy of undetermined significance (MGUS), immunoglobulin light chain (AL) amyloidosis, and lymphoplasmacytic lymphoma, also termed Waldenström macroglobulinemia.

Multiple myeloma is caused by the proliferation of neoplastic plasma cells in the bone marrow. Such cells usually produce an immunoglobulin protein that can be detected in serum (paraprotein or M component) or urine (immunoglobulin light chains, or Bence Jones protein). The major clinical features of myeloma include anemia, lytic bone lesions, hypercalcemia, and renal failure. Patients become prone to infection, fractures, and suffer from fatigue and pain.

Like myeloma, AL (immunoglobulin light chain or primary systemic) amyloidosis originates in the bone marrow plasma cell. AL amyloidosis is about one-third as common as myeloma, but can occur with myeloma in 10-15% of patients. In AL amyloidosis, the light chains synthesized by the clonal plasma cells aggregate and form insoluble fibrils that damage various tissues and organs. AL amyloidosis is the most common systemic amyloidosis. Other forms of systemic amyloidosis can be hereditary or secondary to inflammatory diseases.

The clinical features of AL amyloidosis include nephrotic syndrome, congestive heart failure, autonomic and peripheral neuropathy, GI symptoms, bruising or bleeding, and an enlarged tongue. If untreated, most patients will die within 12 to 18 months of diagnosis.

Management of both myeloma and AL amyloidosis targets the abnormal plasma cells in the bone marrow. Therapies for AL amyloidosis are derived from their use in myeloma. However, the organ dysfunction associated with AL amyloidosis affects the tolerability of therapeutic regimens, and survival is worse in AL amyloidosis patients due to organ dysfunction and failure.

## Multiple Myeloma at BMC from 2006-2010: Outcome Data

The Boston Medical Center (BMC) Cancer Care Committee reviewed myeloma cases from a period of five years dating from January 1, 2006, through December 31, 2010, and compared this data with the National Cancer Database (NCDB).

The data shows that the total number of newly diagnosed myeloma cases at BMC rose steadily from nine in 2006, to 16 in 2009, with 12 in 2010 (Figure 1).

The racial distribution of patients with myeloma at BMC is more diverse than the nationwide average. Caucasians comprise 71% of such patients in National Cancer Database (NCDB) data, but only 41% of patients with myeloma at BMC. Of non-Caucasian patients, 59% are African-American at BMC. (Figure 2)

Data on the age of patients at diagnosis shows that at BMC, patients are diagnosed with myeloma at a younger age than is typical nationwide (Figure 3).

At BMC, the five-year survival rate of patients with myeloma is notably higher than national outcomes according to the NCDB, with a five-year survival rate of 43% compared with 32% nationally (Figure 4).

Figure 1  
Myeloma Cases at BMC 2006 – 2010



Figure 2  
Myeloma Cases at BMC – Distribution by Race 2006 – 2010

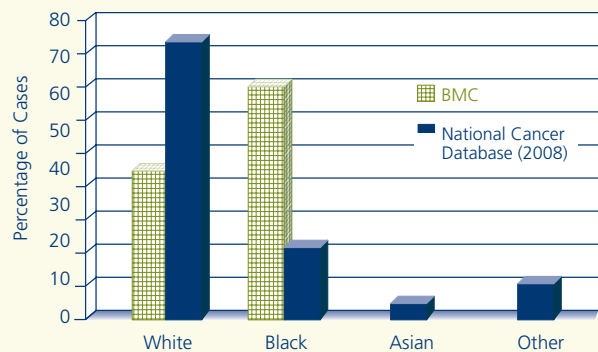


Figure 3  
Myeloma Age at Diagnosis 2006 – 2010

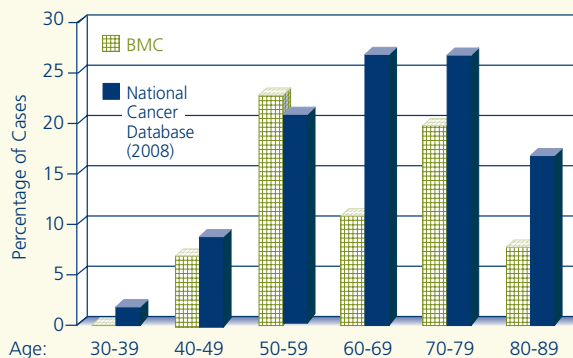
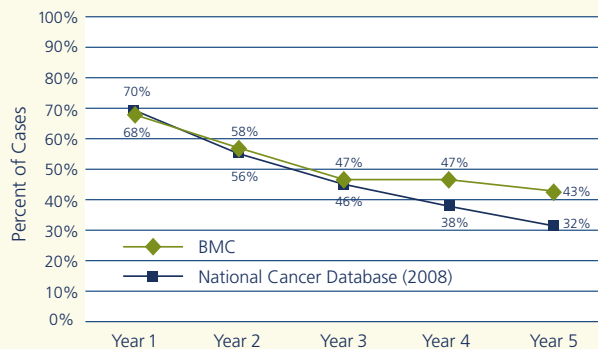


Figure 4  
Myeloma 5-Year Survival Rate 2006 – 2010



## Amyloidosis at BMC from 2006-2010: Outcome Data

BMC reviewed all cases of amyloidosis dating from January 1, 2006, to December 31, 2010, which includes five years of data. The NCDB does not track data for amyloidosis.

At BMC, the annual number of total evaluations performed for amyloidosis increased from 339 in 2006, to 560 in 2010, with a total of 2,172 evaluations over this five-year period. The annual number of new diagnoses of amyloidosis also increased during this period, rising from 149 patients in 2006, to 186 in 2010, with a total of 902 cases over five years. Of these 902 new cases of amyloidosis, 516 were referred for AL amyloidosis.

	Total cases	Total new cases	New AL cases	New non-AL cases
<b>2006</b>	339	149	95	54
<b>2007</b>	360	147	87	60
<b>2008</b>	405	190	113	77
<b>2009</b>	508	230	137	93
<b>2010</b>	560	186	84	102

## Collaborative Approach to Patient Care

Treatment of patients with multiple myeloma and AL amyloidosis targets the underlying clonal plasma cell dyscrasia that is common to both diseases.

The mainstay of therapy for myeloma and AL amyloidosis is chemotherapy. The care of patients with these diseases at BMC is usually coordinated by the hematologist-oncologist, working closely with colleagues in Radiation Oncology and other specialties. Collaboration to optimize patient care also involves many other specialists. For example, a patient with renal complications will see a nephrologist. Patients with bone disease may need orthopedic surgery, radiation therapy, or the assistance of a pain specialist.

At BMC, patient navigators help to coordinate patient care, and aid patients in overcoming barriers to state-of-the-art medical care including insurance issues, language or legal problems, and transportation or childcare assistance. These support services ensure that patients can comply with the optimal treatment for their disease.

>> At BMC, patient navigators help to coordinate patient care, and ... ensure that patients can comply with the optimal treatment for their disease. <<

The Amyloid Treatment and Research Program is an international leader in the development and delivery of treatment for amyloidosis. Its approach is a model of integrated, multidisciplinary medicine. Providing highly individualized, cutting-edge care, its team of practitioners guides the patient through a three-day evaluation and therapeutic options that may vary from oral drug regimens to high-dose chemotherapy and autologous stem cell transplantation as well as clinical trials.

While most patients treated for multiple myeloma at BMC live nearby, individuals with AL amyloidosis travel from throughout the United States and overseas to receive their care at BMC.

Because amyloidosis affects multiple organs, diagnosis and treatment require clinicians with diverse expertise. Amyloid internists coordinate treatment plans in consultation with BMC's experts in cardiology, endocrinology, hematology, nephrology, neurology, otolaryngology, pathology, pulmonary medicine, psychiatry, radiation oncology and rheumatology.

BMC clinicians support patients throughout evaluation, treatment and follow up. Care is coordinated by Department of Medicine Clinical Instructors Rosemary O'Connell, MD and Andrew Cowan, MD. The team also includes a dedicated social worker, patient navigator, massage and acupuncture therapists, medical genetics consultants and clinical trials staff. BMC's deeply collaborative approach contributes to outstanding results in patient outcomes and safety.

From bench to bedside, BMC is at the forefront of care for patients coping with these complex diseases.

## Multi-Disciplinary Amyloid Team

### HEMATOLOGY

**David Seldin, MD, PhD**, Section Chief, Hematology and Oncology, Professor of Medicine and Microbiology

**Vaishali Sanchawala, MD**, Clinical Director of Stem Cell Transplant Program, Section of Hematology and Oncology, Professor of Medicine

**J. Mark Sloan, MD**, Section of Hematology and Oncology, Assistant Professor of Medicine

### CARDIOLOGY

**Frederick Ruberg, MD**, Director, Advanced Cardiac Imaging Program, Section of Cardiovascular Medicine, Assistant Professor of Medicine

**Hans Meier-Ewert, MD**, Section of Cardiovascular Medicine, Assistant Professor of Medicine

### ENDOCRINOLOGY

**Sonia Anantkrishanan, MD**, Section of Endocrinology, Diabetes and Nutrition Hematology, Assistant Professor of Medicine

### NEPHROLOGY

**Laura Dember, MD**, Sections of Hematology and Oncology and Nephrology, Assistant Professor of Medicine

**Andrea Havasi, MD**, Section of Nephrology, Assistant Professor of Medicine

**Lauren Stern, MD**, Section of Nephrology, Assistant Professor of Medicine

### NEUROLOGY

**Janice Wiesman, MD**, Department of Neurology, Assistant Professor of Neurology

### OTOLARYNGOLOGY

**Gregory Grillone, MD, FACS**, Vice Chairman, Department of Otolaryngology-Head and Neck Surgery, Director, Center for Voice and Swallowing, Associate Professor of Otolaryngology-Head and Neck Surgery

### PATHOLOGY

**Carl O'Hara, MD**, Chief, Section of Laboratory Medicine, Professor of Pathology and Laboratory Medicine

**Karen Quillen, MD, MPH**, Medical Director, Blood Bank, Associate Professor of Medicine and Pathology and Laboratory Medicine

**Marianna Ruzinova, MD**, Medical Director, Hematology Laboratory, Assistant Professor of Pathology and Laboratory Medicine

### PULMONARY MEDICINE

**John Berk, MD**, Clinical Director, Amyloid Treatment & Research Program, Associate Professor of Medicine

### PSYCHIATRY

**Isidore Berenbaum, MD**, Associate Director C/L Psychiatry, Assistant Professor of Psychiatry

### RADIATION ONCOLOGY

**Minh Tam Truong, MD**, Clinical Director, Department of Radiation Oncology, Assistant Professor of Radiation Oncology

### RHEUMATOLOGY

**Caryn Libbey, MD**, Section of Rheumatology, Clinical Associate Professor of Medicine

**Martha Skinner, MD**, Amyloid Program Director of Special Projects, Section of Rheumatology, Professor of Medicine

### UROLOGY

**Mark Katz, MD**, Department of Urology, Assistant Professor of Urology



## Diagnosis

BMC has developed highly precise techniques for assessing and diagnosing patients for multiple myeloma and AL amyloidosis. Diagnosis is highly dependent upon the analysis of the bone marrow and other tissue biopsies by a qualified hematopathologist.

At BMC, Dr. O'Hara heads this program in the Department of Pathology and Laboratory Medicine. For diagnosis, his department uses flow cytometry, immunohistochemistry, *in situ* hybridization, electron microscopy, molecular diagnostics, and more standard histology techniques, for diagnosis of BMC patients and for confirmation of cases from other hospitals all over the country.

### Diagnosing multiple myeloma

Multiple myeloma is a plasma cell neoplasm resulting from the expansion of a clone of malignant plasma cells that primarily occupy the bone marrow.

The morphology of a bone marrow core and marrow aspirate smears play a pivotal role in establishing a diagnosis of myeloma. While the normal bone marrow contains a small population of mature plasma cells (about 3-to-5% of marrow cellularity), plasma cells in myeloma are often characterized by cytological immaturity and high cellularity (usually in excess of 10%), and they usually appear as clusters and aggregates.

Plasma cells can be enumerated with aspirate smears and flow cytometry. However, a more accurate representation of the *in-situ* state is yielded by a core biopsy using an immunohistochemical stain for the plasma cell associated antigen CD138. Because this surface antigen is expressed only on plasma cells and not on other hematopoietic elements, its stain produces a more reliable count.

Once the volume has been established, the next parameter to assess is the clonality of the plasma cells, which is indicated by the presence of kappa and lambda light chain immunoglobulins. The process is most likely reactive (non-malignant) if a population of plasma cells contains both kappa and lambda positive cells. Conversely, if all the plasma cells express only one light chain (kappa or lambda), then the process is monoclonal and indicative of malignancy.

BMC's hematopathology lab uses an *in situ* hybridization technique to detect immunoglobulin light chains. This practice results in cleaner, crisper staining that greatly facilitates interpretation. Once the plasma cells are enumerated and found to be monoclonal in the bone marrow, the results are interpreted in the light of quantitative and qualitative serum and urine immunoglobulin levels, other laboratory data (serum calcium, hemoglobin concentration), and radiographic findings. This combined data is assessed together with clinical information to arrive at a diagnosis of multiple myeloma.

### Diagnosing amyloidosis

The diagnosis of amyloidosis relies on the demonstration of extracellular homogeneous eosinophilic deposits in tissues and organs throughout the body. The extent of deposition may vary from focal involvement of blood vessels to massive replacement of organs such as the spleen, liver and heart.

Amyloid has a non-specific eosinophilic appearance when stained with standard stains. However, when viewed by electron microscopy, amyloid fibrils have a very distinctive ultrastructural appearance that is a diagnostic indicator. The gold standard for diagnosing amyloidosis is the definitive demonstration on a tissue biopsy or fat pad aspirate of positive Congo red staining that produces apple green birefringence under polarized light.

The Congo red stain identifies all subtypes of amyloid fibrils and does not distinguish one type from another. Other modalities that are useful for determining subtypes include immunohistochemistry and an immuno-gold electron microscopy.

## Treatment and Clinical Trials

Treatment of myeloma and AL amyloidosis is directed toward the underlying plasma cell dyscrasia. The goal is to eradicate the production of the monoclonal protein in myeloma as well as the precursor protein of the amyloid fibrils in AL amyloidosis.

Standard treatment consists of oral melphalan and steroids. However, rates of remission are low with these drugs. Novel therapies with immunomodulatory drugs such as thalidomide and lenalidomide,

or proteasome inhibitors such as bortezomib, have yielded superior results and transformed the therapeutic landscape of myeloma. In studies pioneered by investigators at BMC, the same drugs are proving equally useful for patients with AL amyloidosis. Second- and third-generation analogs are entering into trials.



Clinical trials have proven to be the best way to identify effective new therapies, and are often the only way to gain access to new drugs. In these programs, patients are treated with the best available standard therapy, and new agents are either compared to or added to the standard. BMC investigators participate in clinical trials designed by national cooperative groups such as the Southwest Oncology Group, the Radiation Therapy Oncology Group, and other agencies. For the rare disease AL amyloidosis, many of the trials are designed by investigators at BMC.

In the mid-'90s, BMC pioneered pilot clinical trials of high dose chemotherapy and autologous peripheral blood stem cell transplantation for patients with AL amyloidosis. This aggressive treatment has improved outcomes for patients, raising rates of remission and overall survival as well as increasing the frequency of disease-free survival.

Between 2004 and 2010, BMC led a successful clinical trial through Southwest Oncology Cooperative National Group that applied this modality to patients with AL amyloidosis at more than 30 medical centers. BMC also pioneered administration of this intensive protocol in an outpatient day hospital setting, where most patients at BMC receive their treatment. Outpatient treatment keeps patients active, comfortable and away from the hospital environment unless absolutely necessary for their care.

>> For the rare disease AL amyloidosis, many of the trials are designed by investigators at BMC. <<



## Autologous Stem Cell Transplant Program

The BMC Autologous Stem Cell Transplant Program treats patients with AL amyloidosis in collaboration with the Amyloid Treatment and Research Program at the BU School of Medicine.

Under the clinical direction of Dr. Sanchorawala, the BMC Autologous Stem Cell Transplant Program maintains accreditation through the Foundation for the Accreditation of Cellular Therapy (FACT). The program has performed more than 640 transplants, 82% for patients with AL amyloidosis and 6% for patients with multiple myeloma. Patients with both multiple myeloma and AL amyloidosis accounted for 3% of the transplants.

### Stem cell harvest and plasmapheresis in multiple myeloma

At BMC, stem cell harvest and plasmapheresis are usually conducted as outpatient procedures over several separate sessions.

Before undergoing treatment, a patient with multiple myeloma or AL amyloidosis must have a high hematopoietic stem cell count in their bloodstream. Growth factors are administered to raise the stem cell count by injection once a day for three days prior to stem cell collection. The patient is carefully monitored for such side effects as low-grade fever, bone and muscle pain and fluid accumulation.

When treatment begins, a large intravenous catheter is inserted in the patient's upper chest. The catheter is the conduit for the entire stem cell transplant process, starting with stem cell collection and continuing with chemotherapy, infusion of stem cells, transfusions, and administration of intravenous fluids and antibiotics.

The patient is connected to an apheresis machine, which is similar in size and function to a dialysis machine. The patient's blood travels through the intravenous catheter into the machine, where a

centrifuge separates out stem cells. While stem cells are collected into a bag, the rest of the patient's blood, including red blood cells, returns to the patient via the catheter. Once underway, this process takes about five-to-six hours.

The bag of stem cells is taken to the stem cell processing lab in the blood bank, where they are mixed with preservative solutions and frozen. A small sample is also taken to count the number of stem cells obtained in the session. Patients usually undergo two sessions to provide enough stem cells for the transplant.

On the day of the transplant, the stem cells are thawed at the bedside and immediately re-infused into the patient, who may experience mild and readily treated side effects such as nausea, flushing and breathing irregularities.

Plasmapheresis is an option for a patient whose multiple myeloma presents with acute kidney failure. This procedure also employs the apheresis machine and central venous catheter. The centrifuge separates out the plasma in the patient's blood to remove the abnormal protein that is damaging the kidneys, and can be effective in selected patients, when used in combination with other treatments.

## Radiation Oncology

At BMC, radiation oncology is integral to the management of multiple myeloma and localized amyloidosis.

Radiation therapy provides a useful palliative treatment to patients with multiple myeloma, who often experience severe bone pain. It can also be effective in treating solitary plasmacytoma. A radiation dosage of 20-30 Gy over two weeks is delivered to control the pain of bone lesions associated with myeloma. Treatment of solitary plasmacytoma comprises 45 Gy over five weeks.



Since low-dose radiation induces plasma cell apoptosis in other plasma cell dyscrasias and lymphoproliferative disorders, radiation treatment may also have applications in localized amyloidosis. By eliminating amyloidogenic plasma cells, radiation can arrest amyloid production and prevent disease progression or lesion recurrence.

A multidisciplinary team at BMC has demonstrated the role of low-dose radiation (20 Gy over two weeks) for patients with localized amyloidosis in the laryngeal and tracheobronchial airways. Small populations of clonal plasma cells located outside the airway are regarded as the source of amyloidogenic light chain immunoglobulin production that stimulates amyloid formation. Radiation prevents progressive amyloid deposition, marginally increasing pulmonary function without late morbidity.

A BMC team consisting of Drs. Berk, Grillone and Truong (Departments of Pulmonary Medicine, Otolaryngology/Head and Neck Surgery, and Radiation Oncology, respectively) recently published a report on their effective usage of low-dose radiation to treat progressive airway amyloidosis.

## Nursing

Most individuals diagnosed with multiple myeloma and AL amyloidosis receive treatment as outpatients. RNs in the BMC Hematology/Oncology Clinic provide patients with care, support and education throughout treatment.

A primary nurse is assigned to each patient. The nurse maintains a continuous relationship with the patient during the entire process.

Primary nurses work closely with their patients. They administer chemotherapy and other medications as well as IV fluids and draw patients' blood for lab analysis. They become familiar with patients' responses to treatment and monitor them closely for subtle changes. Before discharge, the nurse provides extensive education to the patient and family about medications, adjustments to daily routines and techniques to avoid infection and identify its symptoms.

If patients are hospitalized, inpatient nurses monitor them, administer chemotherapy if necessary, and continue the support and education of patients and their families.

An RN with advanced training as a Nurse Practitioner coordinates care and support for patients undergoing stem cell transplantation.

## Integrative Medicine

Integrative medicine practices have been shown to reduce cancer-related symptoms such as pain, anxiety, nausea and fatigue. The Program for Integrative Medicine and Health Care Disparities in the BMC Department of Family Medicine combines conventional medical treatments with evidence-based complementary therapies.

Led by Robert Saper, MD, MPH, Director of Integrative Medicine and Associate Professor, Department of Family Medicine, the program offers patients and staff a spectrum of evidenced-based integrative approaches to care. BMC also is investigating the benefits of integrative care to patients with cancer with ongoing research.

Through an educational partnership with the Cortiva Massage School, free therapeutic massage is available to cancer patients and staff. At the Moakley Building, where BMC conducts much of its cancer care, registered yoga teacher Anna Dunwell holds two free weekly yoga classes and licensed acupuncturist Ellen Highfield offers acupuncture services to patients with cancer. In 2010, 249 acupuncture treatments were provided to patients in various stages of cancer survivorship. The program is partially supported by a grant from the Tides Foundation through the New England School of Acupuncture.



Patients also have access to complimentary Tai Chi and music therapy sessions and a weekly mediation group. Participants have gained notable clinical benefits, reporting decreases in nausea, pain, depression, anxiety and fatigue.

Services to individual patients complement group activities. Assistant Director of Integrative Medicine and Assistant Professor, Department of Family Medicine, Paula Gardiner, MD, MPH, offers consultations to patients that focus on stress management, nutrition and coordination of complementary therapies.

>> In 2010, 249 acupuncture treatments were provided to patients in various stages of cancer survivorship. <<

## Expert Pharmaceutical Guidance

BMC's board-certified oncology pharmacists Bhavesh Shah, RPh, and Radhika Sane, Pharm D, work side-by-side with the Section of Hematology and Oncology to optimize cancer related pharmacotherapy. These specialized pharmacists interpret and manage complex chemotherapy drug dosing, drug-drug interactions and drug toxicity on behalf of patients. In addition to their pharmacotherapy expertise, they counsel patients on appropriate side-effect management and help facilitate safe administration of medication.

## Patient Support Services

The BMC Cancer Support Services Program provides a comprehensive set of services to help patients focus on combating and coping with their disease. Designed to improve long-term outcomes and survivorship, these services address an array of medical, social, economic and emotional needs.

BMC currently offers 25 support groups and educational workshops for patients diagnosed with cancer and their caregivers. These activities include a weekly support group for amyloid patients and monthly support groups for patients with multiple myeloma, lymphoma and leukemia. Exercise classes vary from Healthy Steps/Lebed and gentle yoga to Qigong/Tai Chi and Zumba. Other patient resources include the services of social workers, nutritionists, patient navigators and interpreters as well as assistance with transportation, childcare and treatment coordination.

### Patient assistance program

BMC recognizes that the economics of cancer treatments can have significant financial impact on patients and their families. BMC has implemented a hematology/oncology medication access program to provide high-quality care to every patient, including those who cannot afford their medications. This program helps patients acquire medications directly from the pharmaceutical company or through appropriate chronic disease funds.

### Patient navigators

BMC's patient navigators function like case managers, coordinating care and guiding patients through complex diagnostic and treatment plans. They help schedule services among diverse medical personnel, develop treatment calendars, arrange translation or interpretation services, facilitate transportation to and from medical visits, call patients who have skipped appointments, and offer support and encouragement.

Of the four dedicated patient navigators in the Section of Hematology and Oncology, one navigator works closely with patients diagnosed with hematologic malignancies, including multiple myeloma. Nurses provide navigation services to the many out-of-state patients with AL amyloidosis who participate in BMC's clinical trials and Autologous Stem Cell Transplant Program.

Many BMC patients cope with such issues as insurance gaps, financial stresses, lack of childcare and transportation, low literacy levels and language barriers. These factors can compound the challenges of patients and their families as they undergo treatment. BMC's navigator program helps such patients identify and overcome obstacles to care, improve treatment compliance and decrease the "no show" rate. The program also develops disease algorithms that streamline and expedite patient care.

## Research to Advance Detection, Diagnosis and Cure

At BMC, patients with AL amyloidosis receive state-of-the-art treatment by specialists who are renowned both as clinicians and researchers. BMC's translational research informs patient care and its clinical trials expand patients' therapeutic options.

### Translational research

At BMC, patients with AL amyloidosis are evaluated and treated in coordination with the Amyloid Treatment and Research Program of the Boston University School of Medicine. This unique patient population benefits from the program's translational research into therapies for plasma cell dyscrasias. In turn, their participation advances this critical research.

Founded more than 50 years ago, the Amyloid Treatment and Research Program is a world-renowned leader in research and patient care. One of only a handful of major centers globally dedicated to the study and treatment of AL amyloidosis, the program has pioneered many advances in understanding and treating this rare disease.

Over five decades, the program's affiliated investigators have made seminal discoveries about the biochemical and biophysical properties of amyloid proteins. During the last 20 years, the program's research has focused on the development of new therapies. While conducting clinical trials of stem cell transplantation and other anti-plasma cell therapies, investigators have worked to develop pre-clinical immunotherapy, animal model systems for new anti-fibril therapies, and new biomarkers and imaging approaches to help patients with this rare myeloma-related condition.

In the arena of immunotherapy, David Sherr, PhD, Director, Immunology Training Program and Professor of Environmental Health, and his colleagues have developed peptide vaccines based

upon the unique sequences of amyloidogenic light chains and a plasma cell transcription factor, Blimp-1. These vaccines have been tested in mice and may eventually be used in patients.

The laboratory of David Seldin, MD, PhD, has engineered transgenic mice that develop human light chain amyloid in their stomachs. This property makes the mice useful for testing oral therapeutic agents.

Biomarkers measure disease activity and provide clues to the diagnosis of amyloidosis and potential mechanisms of tissue damage. Lawreen Connors, PhD, Director of Gerry Amyloid Laboratory, Section of Cardiovascular Medicine, Assistant Professor of Medicine, and colleagues demonstrated that the chaperone clusterin is reduced in the circulation of patients with amyloid cardiomyopathy. Flora Sam, MD, Section of Cardiovascular Medicine, Associate Professor of Medicine, has identified alterations in matrix metalloproteinases and their inhibitors, biomarkers that may also play a role in remodeling in amyloid cardiomyopathy.

Diagnostics will improve with better imaging techniques to identify amyloid involvement of organs. Frederick Ruberg, MD, has found that patients with amyloid deposits in the heart have a characteristic pattern of enhancement with gadolinium contrast on magnetic resonance imaging. James Hamilton, PhD, Director, High Field NMR and MRI Center and Professor of Physiology and Biophysics and Stephan Anderson, MD, Associate Professor, Department of Radiology, are expanding this modality to other organs using novel analytical algorithms.



## Clinical trials

The BMC Clinical Trials Program, co-directed by Kathleen Finn, NP, and Timothy Cooley, MD, Physician Director, Cancer Clinical Trials Program, Section of Hematology and Oncology, and Associate Professor of Medicine, offers patients new and promising options for treatment.

BMC leads in the enrollment of minority populations in clinical trials, which bring the most advanced care to patients with cancer. At BMC, 9% of newly diagnosed cancer patients enroll in

cancer clinical trials, a rate that exceeds the national average by 300%. About 48% of the enrollees represent minority populations.

Weekly joint conferences of the Autologous Stem Cell Transplant Program and Amyloid Treatment and Research Program evaluate patients for clinical trial eligibility. The former group considers candidates for high-dose chemotherapy and the latter group reviews patients diagnosed with amyloidosis.

Clinical research studies at BMC related to AL amyloidosis and multiple myeloma are listed below.

## Clinical Trials

### AMYLOIDOSIS

#### *Ongoing:*

**IRB #H-26320:** Phase II Trial of MRD (Melphalan, Lenalidomide and Dexamethasone) for Patients with AL Amyloidosis

**IRB #H-28441/X50292:** Phase II Trial of Induction Therapy with Bortezomib and Dexamethasone Followed by High-Dose Melphalan and Stem Cell Transplantation in Patients with AL Amyloidosis

**IRB #2011-0284/Millennium #C16007:** An Open-Label, Dose-Escalation, Phase 1 Study of the Oral Formulation of MLN9708 Administered Weekly in Adult Patients With Relapsed or Refractory Light Chain (AL) Amyloidosis Who Require Further Treatment

**IRB #2006-1918/Merck V212:** A Phase III, Double-Blind, Randomized, Placebo-Controlled, Multicenter Clinical Trial to Study the Safety, Tolerability, Efficacy, and Immunogenicity of V212 in Recipients of Autologous Hematopoietic Cell Transplants (HCTs)

#### **IRB #H-31166/CTSU #E4A08:**

A Randomized Phase III Trial of Melphalan and Dexamethasone (MDex) versus Bortezomib, Melphalan, and Dexamethasone (BMDex) for Untreated Patients with Systemic Light Chain (AL) Amyloidosis Ineligible for Autologous Stem-cell transplantation

#### *Recently completed:*

**IRB #H-22603/SCT #0156:** Phase II Trial of Second Autologous Transplantation in AL Amyloidosis

**IRB #H 22939/SWOG #S0115:** A Ph II Trial Evaluating Modified HD Melphalan (100 mg/m<sup>2</sup>) and Auto SCT for AL amyloidosis and/or High Risk Pts w/MM

**IRB #H-23235:** Phase II Trial of Immunomodulatory Drug CC-5013 for Patients with AL Amyloidosis

#### *Upcoming:*

**IRB #H-38012/Pomalidomide:** A Phase I/II Trial of Pomalidomide and Dexamethasone in Subjects with Previously-Treated AL Amyloidosis (pending)

### MULTIPLE MYELOMA

**IRB #H-27430/SWOG #S0777:** A Randomized Phase III Trial of Lenalidomide and Low Dose Dexamethasone (LLD) Versus Bortezomib, Lenalidomide and Low Dose Dexamethasone (BLLD) for Induction, in Patients with Previously Untreated Multiple Myeloma Without an Intent for Immediate Autologous Stem Cell Transplant

**IRB #2006-1918/Merck V212:** A Phase III, Double-Blind, Randomized, Placebo-Controlled, Multicenter Clinical Trial to Study the Safety, Tolerability, Efficacy, and Immunogenicity of V212 in Recipients of Autologous Hematopoietic Cell Transplants (HCTs)



## Cancer Data Registry

The BMC Cancer Registry, under the guidance of the Cancer Care Committee and directed by Ruth Flaherty, CTR, maintains a database of cancer data for about 15,000 cancer cases. This database contains each patient’s demographic, diagnostic, treatment and yearly follow-up information.

The Cancer Registry analyzes and disseminates this data for hospital cancer studies, marketing reports and submissions to state, regional and national databases. Its reports include monthly submissions to the Massachusetts Cancer Registry and annual submissions to the National Cancer Database.

In 2011, the Cancer Registry worked with the Cancer Care Committee at large to prepare its survey for re-accreditation by the American College of Surgeons Commission on Cancer as a Teaching Hospital Cancer Program. Following the survey, which was conducted on November 14, 2011, BMC received three-year re-accreditation with commendation.

### 2010 Cancer Registry Data

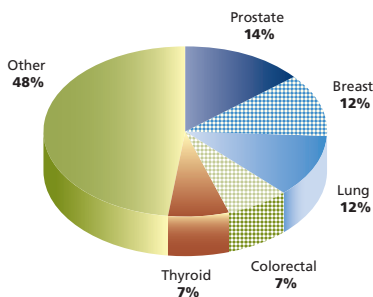
In 2010, the BMC Cancer Registry accessioned 1,295 new cancer cases. Of these cancer cases, 651 were male and 644 were female. Major sites continue to be prostate, breast, lung, colorectal

and thyroid cancers. Age distribution data show that 68% of new cases are patients between 40 to 70 years of age. Race distribution figures indicate that 57% of patients are Caucasian and 43% are from minority populations.

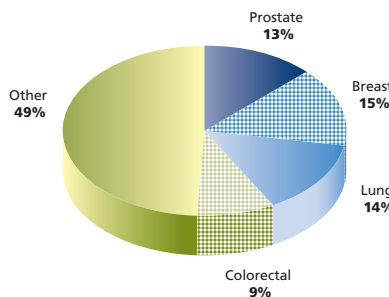
### Top Cancer Sites in 2010

	Boston Medical Center	Massachusetts	American Cancer Society
<b>Prostate</b>	14% (182)	13%	14%
<b>Breast</b>	12% (152)	15%	14%
<b>Lung</b>	12% (149)	14%	15%
<b>Colorectal</b>	7% (91)	9%	9%
<b>Thyroid</b>	7% (89)	N/A	3%

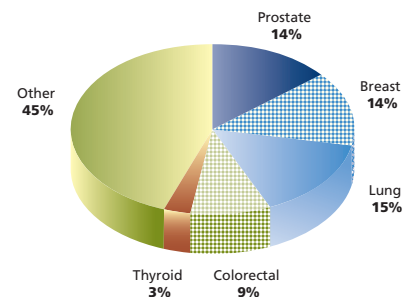
**Boston Medical Center**  
*Top Cancer Sites 2010*



**Massachusetts**  
*Top Cancer Sites 2010*



**American Cancer Society**  
*Top Cancer Sites 2010*



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