

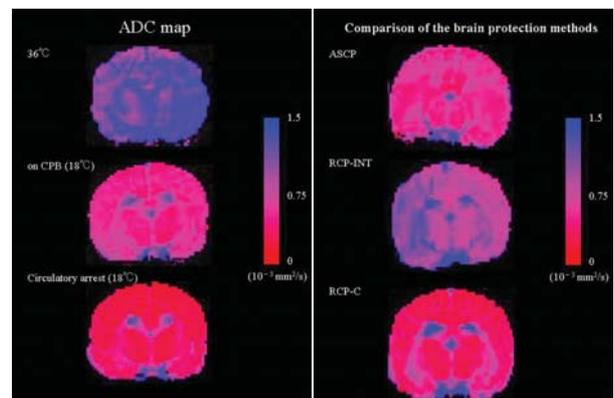
# Surgical Sciences

## Cardiovascular Surgery, Thoracic Surgery

<http://ctstokyo.umin.ne.jp/>

We are leading in Japan by annual surgery case volume of 700. New knowledge and techniques are actively applied clinically. Many clinical research projects are going on along with routine clinical activities. Our laboratories have been also carrying out a large variety of basic research.

- Clinical research
  - Brain and spinal cord protection in thoracic aortic surgery
  - Minimally invasive cardiac and thoracic surgeries
  - Valve or vascular tissue allograft transplantation
  - Ventricular assist device for end-stage heart failure
  - Pathophysiology of thymic epithelial neoplasms
- Basic and experimental research
  - Development of myocardial regeneration therapy
  - Analysis of resistance to infection of tissue allograft
  - Analysis of suppressor gene of lung cancer



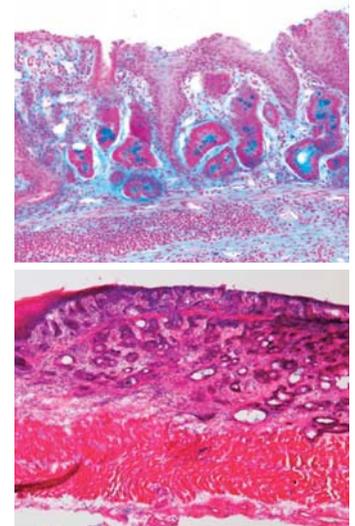
MRI diffusion-weighted images of brain by various brain perfusion techniques

## Gastrointestinal Surgery

<http://todai3ge.umin.jp/>

Our research activities range from basic topics to clinical ones with close inter-connections. Basic research topics encompass underlying molecular mechanisms and the regulation of carcinogenesis, progression, metastasis and prevention of gastrointestinal cancer. Clinical research topics include the establishment of tailored treatment strategies from a patients-by-patient point of view, which ultimately provide a better quality of life while improving survival quality.

- Carcinogenesis, progression, metastasis and prevention of gastrointestinal cancer
  - Inflammation and gastrointestinal carcinogenesis (gastroduodenal reflux, H. pylori infection)
  - Are cancer cells derived from bone marrow?
  - Earlier detection of cancer and micrometastasis by new genetic markers
  - Roles of epigenetic alteration (DNA methylation) in gastrointestinal carcinogenesis
  - Carcinogenic analysis with murine esophageal reflux model
- Establishment of tailored treatment strategies
  - Less invasive treatment of early cancer by laparoscopic (assisted) surgery
  - Sentinel node navigation surgery for early cancer
  - Extended radical treatment of advanced cancer
  - Induction of neoadjuvant chemotherapy and improvement of survival
  - Estimation of chemotherapy effects by new bio- and genetic-markers
  - Alternative gastrointestinal reconstruction and estimation of the results



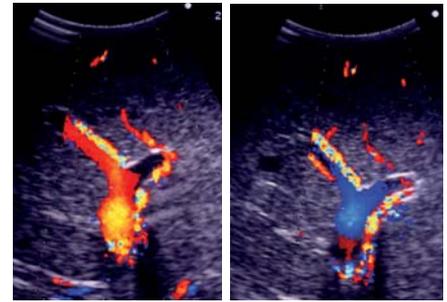
Barrett's esophagus and Cancer in reflux model mouse

## Hepatobiliary Pancreatic Surgery

<http://square.umin.ac.jp/hbp-t/index21.htm>

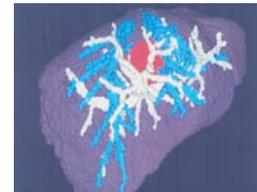
We constantly perform nearly 200 hepatectomies every year on patients with hepatobiliary malignancies including hepatocellular carcinoma and metastatic liver tumors. The surgical results can be classified as amongst the highest ranking in the world. In order to improve the surgical outcome for hepato-biliary-pancreatic malignancies, we conduct wide areas of research such as analysis of prognostic factors for liver malignancies, evaluation of liver hemodynamics using ultrasonography, liver ischemia/reperfusion injury, and liver regeneration.

- The development of a radical and safe operative procedure for hepato-biliary malignancies
- The analysis of genetic abnormalities in hepatocellular carcinoma
- Development of new methods for the evaluation of liver functional reserve
- The evaluation of hemodynamics in the congested liver using ultrasonography
- Study of the effect of ischemic preconditioning on liver normothermic ischemia/reperfusion



Color flow mapping of intraoperative Doppler ultrasonography before division of the middle hepatic vein. Portal flow was hepatopetal (shown in red).

Color flow mapping of intraoperative Doppler ultrasonography after transection of the middle hepatic vein. Portal flow was hepatofugal (shown in blue) in the veno-occlusive area.



Preoperative 3-D image of the liver constructed by simulation software. Accurate anatomy of vasculature and tumor location is analyzed.

## Urology

<http://www.h.u-tokyo.ac.jp/urology/>

We constantly perform more than 1,400 urological surgeries a year, including nephrectomy, cystectomy and prostatectomy, with increasing trend of laparoscopic maneuvers and brachytherapy for organ confined prostate cancer. Surgical or Non-surgical means are employed for non-cancer diseases including renal transplantation, urinary dysfunction, urinary incontinence, urolithiasis and male infertility. With regard to laboratory research, not only oncology but also JC virus, PCK disease and vascular biology are now under extensive investigation.

- Tailor medicines on estramustine phosphate (EMP) has been investigated for newly diagnosed advanced prostate cancer (Fig.1)
- JC viral genomic analyses and its distribution in the world
- Estrogen receptor beta and its metabolic cascade analysis
- Hormonal regulation of prostatic proliferation and atrophy
- Human E&H-cadherin correlation with invasiveness of transitional cell carcinoma and prostate cancer
- Oncolytic viral therapy using HSV-1 (Fig.2)
- PCK disease and genetic analysis
- Urolithiasis: ion channels membrane transport (NaDC-1)
- Vascular biology and erectile dysfunction (ED)
- Fluorescence in situ hybridization (FISH) flow cytometry
- Immunotherapy for renal cancer by IL-2 blocking with anti-IL-2-mAb

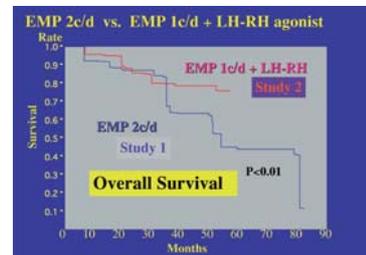


Fig. 1 Overall Survival; EMP 2Cp versus EMP 1Cp + LH-RH agonist

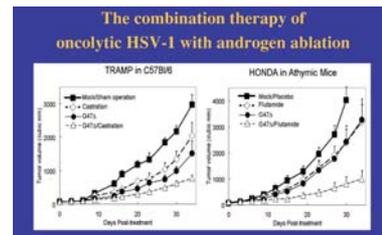


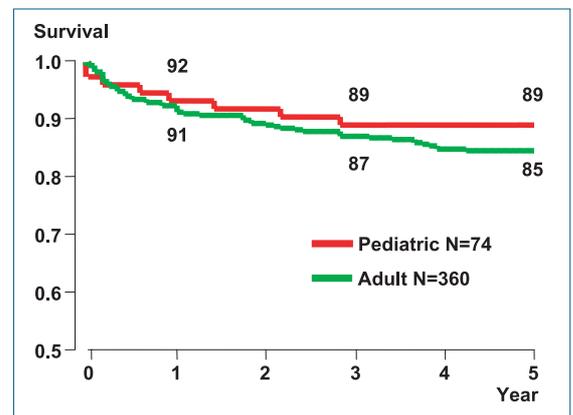
Fig. 2 The combination therapy of oncolytic HSV-1 with androgen ablation led to significantly enhanced inhibition of the tumor growth.

## Artificial Organ and Transplantation Division

<http://www.h.u-tokyo.ac.jp/patient/depts/1512ishokugeka.html>

We are doing the clinical studies about liver transplantation for end staged liver diseases. We have performed 434 living donor liver transplantation and 9 deceased donor liver transplantation until June, 2009.

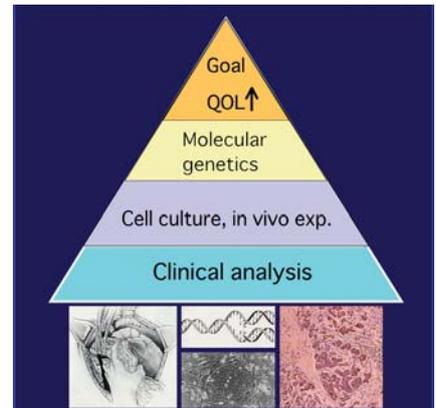
- Surgical technique of liver transplantation
- Diagnosis and treatment of acute rejection
- Diagnosis and treatment of postoperative infection



The 5-year survival rate for adult cases was 85%, which is significantly superior to that of the national data (70%)

We had a great deal of experience in treating patients with various cancers and vascular diseases, and we have performed much research on carcinogenesis, cancer metastasis, immunology, atherosclerosis, angiogenesis and vascular regeneration. Based on the research results, we are trying to identify the best way to treat each patient with the least surgical stress.

- Development of the novel and order-made therapy for cancer
  - Genetic mutation analysis of various cancers
  - Radiosensitivity and chemosensitivity of cancer
  - Intraperitoneal chemotherapy for peritoneal carcinomatosis
  - Immunotherapy using dendritic cells
  - Characterization of tumor vasculature and its therapeutic application
  - Gene therapy for disseminated metastasis
  - Drug development to target the receptor and signal transduction cascade of bioactive lipids
- Development of a novel method to diagnose and treat the vascular diseases
  - Vascular regeneration therapy for atherosclerotic obliterans (ASO)
  - Visualization of atherosclerotic lesions
  - Robotics surgery for vascular diseases

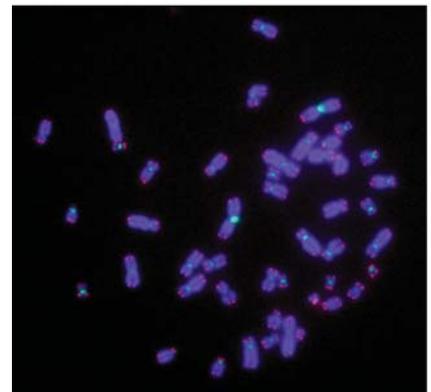


Diagrammatic representation of clinical-oriented research, with the ultimate goal of improving patient QOL

## Metabolic Care and Endocrine Surgery

Our department has two main divisions. Division of surgical metabolism and nutrition performs research on vital response to surgical stress and on metabolic and nutritional care during peri-surgical period. Division of breast and endocrine surgery performs surgery for 230 cases of breast, thyroid and parathyroid tumors a year, and performs research on tumorigenesis, establishment of treatment and prevention of breast and thyroid cancers.

- Surgical metabolism and nutrition
  - Induction of tolerance against surgical stress and endotoxemia
  - Response to endotoxemia through Toll-like receptors
  - Effects of surgical stress on tumor development
  - Gender difference in the response to surgical stress
  - Bacterial translocation during chemotherapy for cancer
  - Establishment of metabolic care and nutritional support team
- Breast and endocrine surgery
  - Roles of nuclear receptor in development of breast cancer
  - Micrometastasis of breast cancer
  - Diagnosis of breast and thyroid tumors by fluorescence in situ hybridization of telomere
  - Expression of insulin-like growth factor 1 receptor in breast cancer tissue as prognostic factor
  - Roles of carbohydrate in breast cancer metastasis
  - Establishment of evaluation on QOL of the patients with breast cancer

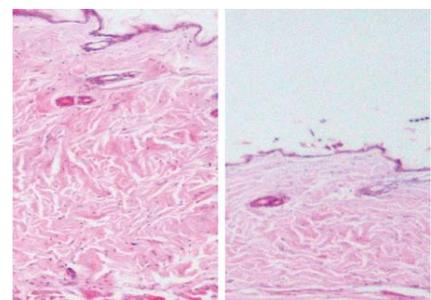


Detection of telomere and centromere by FISH. Fluorescence volume of telomere attenuates with increase of cell division. (red: telomere, green: centromere, blue: chromosome)

## Dermatology

Our department actively performs the following cutting-edge, multifaceted research projects that will be put into clinical practice in the future.

- Molecular mechanisms of immunological abnormalities and skin and lung fibrosis in scleroderma
- Development of novel therapies to scleroderma, including B cell depletion therapy
- Relative contribution of various cell adhesion molecules and chemokines to inflammatory conditions
- Identification of novel autoantibodies and their clinical significance in connective tissue diseases
- New roles of B lymphocytes, especially regulatory roles, in inflammatory disorders
- Immunological abnormalities of atopic dermatitis

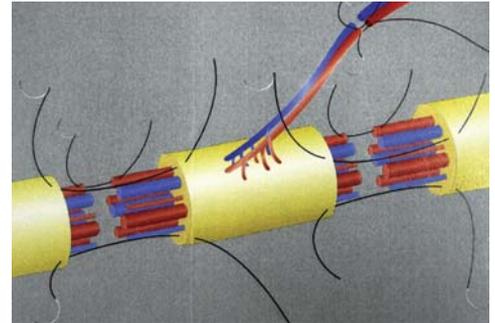


Skin fibrosis induced by bleomycin(left) is inhibited in CD19-deficient mice(right)

## Plastic and Reconstructive Surgery

In our lab, we are investigating the mechanisms of morphogenesis of congenital anomalies using a developmental biological approach. In addition, we are performing extensive research into the clinical application of engineered tissues such as skin, soft tissue, and cartilage. We also have several cosmesis-related projects such as clinical hair regrowth with cultured cells and analysis of skin aging mechanisms.

- Basic Research
  - Mechanisms of embryonic craniofacial morphogenesis
  - Angiogenesis in embryo and vascular malformations
  - Mesenchymal stem cells derived from lipoaspirates
  - Organ engineering with human adult stem cells
  - Hair regrowth with cultured dermal papilla cells
  - Research on aging skin-related factors
  - Regulation of skin aging using hormones and retinoids
  - Regulation of epidermis by factors derived from dermal fibroblasts
- Clinical Research
  - Ultramicrosurgical reconstruction using vascularized tissue transfers
  - Reconstructions for established nerve palsy
  - Esthetic microvascular surgery
  - Mechanism and surgical treatments of lymphedema
  - Vascularized ovarian preservation and transplantation
  - Free vascularized transfers of nerve cells, muscle cells, adiposal cells, and lymphnodes



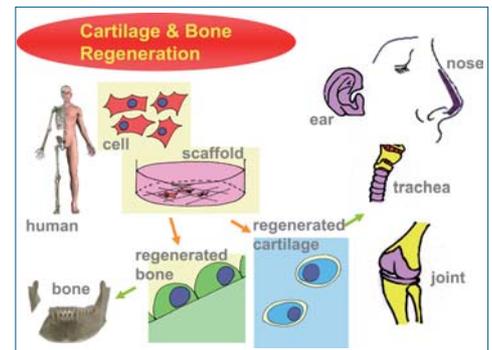
Supermicrosurgical vascularized nerve graft. 100% of Schwann cells within a nerve graft can survive with microvascular anastomosis(0.5mm).

## Oral and Maxillofacial Surgery

<http://plaza.umin.ac.jp/~oralsurg/>

Our laboratory has been performing a wide range of clinically oriented research in oral-maxillofacial disorders such as congenital diseases, jaw deformities and tumors in the oral region. Cartilage and bone regeneration using *tissue engineering techniques* is our main field of research.

- Clinical research:
  - Correction of facial deformity in patients with cleft lip and palate
  - Facial growth in craniofacial anomalies
  - Surgical-orthodontic treatment of dentofacial deformities
  - Evaluation of the treatment outcomes in patients with cleft lip and/or palate
  - Clinical application of artificial bone that displace into bone
  - Implant type artificial bone generated from tissue engineered human chondrocyte
- Basic and experimental research:
  - Cartilage and bone regeneration using the tissue engineering technique
  - Gene analysis of congenital anomalies in the oral and maxillofacial region
  - Effect of free radicals on bone metabolism
  - COX-2 regulation on bone metabolism
  - Development of intelligent type of artificial bone invested with osteogenic differentiation factors
  - Development of tetra pod type micro artificial bone unit



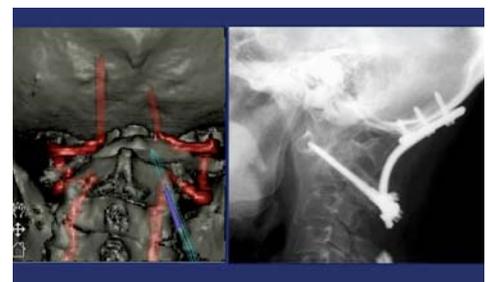
Cartilage and bone regeneration using the tissue engineering technique

## Orthopaedic Surgery

<http://www.h.u-tokyo.ac.jp/ortho/>

Our department was established in 1906 as the first department of orthopaedic surgery in Japan. Since then our efforts have been dedicated to responding to the needs of patients for orthopaedic care and to related research. Our department seeks to elucidate the molecular and genetic backgrounds of bone and cartilage disorders in order to develop groundbreaking treatments for these conditions. At the same time, we are attempting to establish various clinical devices.

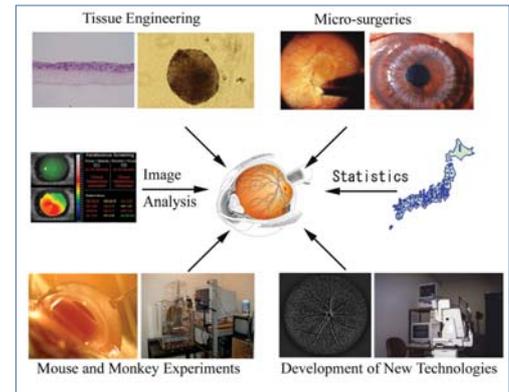
- Systemic and comprehensive study for osteoarthritis
- Bone, cartilage and nerve regeneration
- Regulation of anabolic and catabolic bone metabolism by cytokines
- Molecular mechanism of age-related bone loss
- Molecular mechanism of osteoclast differentiation and apoptosis (RANKL-RANK, INF, Src)
- Gene therapy to control pathological bone destruction (arthritic bone resorption and arthritic joint destruction) using adenovirus vectors
- Non-invasive analyzing system to evaluate the mechanical properties of skeletal system *in vivo* using CT based finite element analyses
- Surgical navigation system with a three-dimensional display and navigation robot



Surgical navigation system

Our department applies cutting-edge technologies and knowledge to diagnosis and treatment of eye diseases. To elucidate pathogenesis and establish more efficient ways of diagnosis and treatment of various refractory eye diseases, basic researches utilizing molecular biological, immunological and/or pharmacological techniques and clinical studies utilizing epidemiological, biostatistical and/or optical methods are conducted. Our efforts are also dedicated to regenerative medicine of the cornea and retina.

- Investigation of primary glaucomas and relating factors
- Development of new methods of glaucoma treatment and validation by RCT
- Investigation of new ocular hypotensive drugs and their mechanism of action by using transgenic or KO mice or experimental glaucoma monkeys
- Investigation of mechanism of neural cell death by using cultured RGCs or retinal glial cells and exploratory search for new neuroprotective agents
- Analysis of ocular circulation in glaucoma and retinal diseases
- Analysis of corneal topography and wave-front analysis of optical aberrations
- Development of tissue-engineered cornea by using cultured stem cells of corneal endothelium and epithelium
- Investigation of molecular mechanism of choroid-retinal neovascularization and new drug delivery system for it utilizing nanotechnology
- Regenerative medicine of the retina using retinal stem cells
- Investigation of immune responses in rejection of transplanted cornea and role of chemokines and receptors in uveitis



## Otorhinolaryngology and Head & Neck Surgery

Our research is composed of both clinical and basic research. Clinical research is conducted by specialized clinics in the hospital, which experience ear diseases and hearing disorders from neonates to adulthood, head and neck cancer, paranasal diseases, olfactory and disorders, vertigo and balance disorders and voice and swallowing disorders. Basic and experimental research into molecular biology, electrophysiology and morphology is conducted in our department's laboratories.

- Clinical research
  - Cochlear implantation in deaf children and their development of hearing, speech and language
  - Surgical correction of congenital microtia and atresia and postoperative radical ears to improve hearing
  - Quality of life in patients with head and neck cancer to restore speech and swallowing function
  - Vestibular research on the oculomotor and balance system and myogenic potential
  - Navigation of the paranasal sinuses and skull base surgery
  - Surgical treatment of voice and swallowing disorders
- Basic and experimental research
  - Molecular biology of the inner ear
  - Molecular biology of epipharyngeal cancer and hypopharyngeal cancer
  - Molecular biology of differentiation and development of inner ear and olfactory epithelium
  - Origins of vestibular myogenic potential
  - Aging and regeneration of olfactory epithelium
  - Binaural hearing

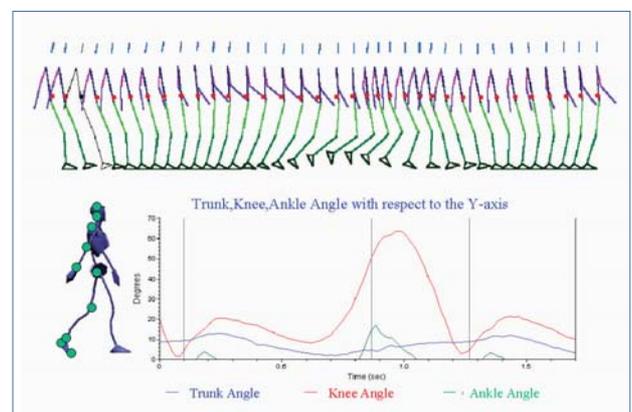


Cochlear implant

## Rehabilitation Medicine

Our research purpose is to improve the provision of a unique and comprehensive rehabilitation service enabling people to develop their full potential and often returning from being a "patient" to being a "person". Clinically oriented studies concentrate on elucidation of the origin of disabilities to cause activity limitation and restriction of participation.

- Gait analysis
  - 3-dimensional image analysis with a infrared camera system
  - Measurements of 3 dimensional ground reaction forces with a force platform
  - Measurements of foot pressures with a computerised pressure sensor
- Clinical research on intractable rare diseases
  - Fibrodysplasia Ossificans Progressiva
  - Congenital Insensitivity to Pain
- Clinical research on congenital limb malformations
- Research on the effect of rehabilitation in palliative care



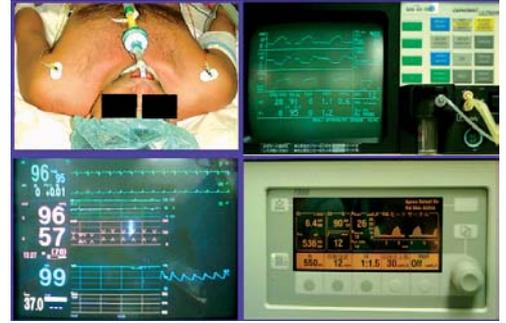
Gait analysis

## Anesthesiology

<http://www.anes.umin.ne.jp/>

We conduct research into various subjects concerned with anesthesia and the pain clinic. There are 6 laboratories in our department. Comprising respiratory, circulatory, nervous and muscular, immune and pain research, and research into anesthetic instruments including monitoring systems.

- **Respiratory system** Our areas of research include changes in pulmonary vascular resistances in pulmonary edema; and influence of anesthetic drugs on the pulmonary system; and pathophysiological changes in neurogenic pulmonary edema
- **Circulatory system** Studies are now being performed on the relationship between the sympathetic nerve system and cardiac function; the influence of inhibitory enzymes upon organic microcirculations; and the ventilation-perfusion distributions during artificial positive pressure ventilation
- **Nervous and muscular system** Studies are now in progress on the mechanism of epidural-spinal anesthesia(using Hanaoka's needle); the influence of anesthetics on the auditory brain stem response; the influence of inhalation anesthetic drugs on the autonomic nervous system; and the pharmacology of neuromuscular blocking agents; and the development of a new monitoring system for neuromuscular blockade
- **Immune system** Themes include the response of immune systems to endotoxins in blood and the influences of anesthetics on hepatic Kupffer cells
- **Pain** We have performed many studies in this area, including the effects of epidural drugs on thermal nociception with different stimulus intensity; the clinical applications of current perceptive thresholds; the mechanism of the analgesic action of laser energy; the clinical applications of drug challenge tests; the examination of the application of epiduroscopic therapy; the analgesic mechanism of hyperventilation; the applications of patient controlled analgesia; the effects of epidural narcotics; and the optimal combination of low dose opioids and inhaled anesthetics
- **Anesthesia machines and other medical equipment** The development of simulators for anesthetic education, and the development of new equipment for tracheal intubation are now in progress



Anesthesia and monitors

## Emergency and Critical Care Medicine

We are collaborating with the School of Engineering, and now concentrating on the development of the infrastructure of emergency medicine including “the Vital Care Network System”, which allows us to manage continuously large numbers of high risk patients. We are also making efforts to improve sterilization and wound healing.

- Vital Care Network System
- Telemonitoring system for prehospital medicine
- High-performance transfer system for the ambulances
- Electrolyzed water
- Autonomic nervous system regulation of the heart

