Morphology-based Visualization Study for Cardiac Arrhythmogenesis

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Cardiac arrhythmia is an abnormal electrical phenomenon arising in the human heart. It is usually assessed clinically by the wave patterns of the electrocardiogram, however, it is often complicated to imagine how the abnormal electrical activities occur and propagate in the heart. In this situation, visualized images of electrical activities in the heart can contribute to our recognition of this non-structural and physiologic phenomenon. We have been experimentally conducting visualization studies of cardiac arrhythmia. First, we identified the macroscopic reentrant circuit in the atria of Langendorff-perfused rat hearts. Clear fluorescent images of the reentrant circuit were obtained using the macro-zoom of a fluorescent microscope and subsequent histologic analysis revealed the intrinsic substrates for the genesis of abnormal slow conduction. Second, we focused on intracellular calcium (Ca^{2+}) dynamics, as its abnormality is relevant to the genesis of cardiac arrhythmias. This method of spatiotemporal optical imaging of intracellular Ca^{2+} dynamics using a spinning disc-based rapid scanning confocal microscope had been established at my previous institute (Kyoto Prefectural University of Medicine, Professor Tetsuro TAKAMATSU and Professor Hideo TANAKA), and we observed various abnormal intracellular Ca^{2+} dynamics in histological images of cardiomyocytes under conditions of electrolyte imbalance and high-frequency electrical stimulation. These morphologic experimental data regarding the genesis of cardiac arrhythmia will provide us useful information for the examination of human autopsy cases who were suffering from various cardiac arrhythmias.

Key words: cardiac arrhythmia, experimental study, histopathology, optical image

Advancement in Lens Reconstruction and Further Improvement of Quality of Vision

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Cataract is a disease that leads to lower vision and is mostly attributable to aging. About 70% of the population is affected by the illness before turning 75, and the number of cataract surgeries per annum in Japan is as high as 1.5 million. There is basically no preventive care, but research has shown that the progression of cataracts may be possibly slowed by the use of ultraviolet-blocking glasses outdoors, the intake of foods high in vitamin C, and stopping smoking. On the other hand, cataract surgery has made it possible to restore vision and has been established as the worldwide standard treatment. Cataract surgery is a highly cost effective surgical treatment since it can improve quality of life and activities of daily living and lower the risk of falls. In the past, cataract surgery aimed at preventing vision loss, but now it can help patients restore their vision to almost as good as in their youth, thanks to advancements in surgical procedures and the evolution of intraocular lenses (IOLs). Multifocal IOLs and IOLs for correcting astigmatism play an important role, as does the emergence of femtosecond laser surgery, which has enabled such IOLs to be precisely fixed using minimally-invasive surgical techniques. The multifocal IOLs that have been used since the early 21st century have two focal points, but the extended depth of
focus lenses and trifocal lenses that have been recently developed can achieve a more sophisticated visual function. Showa University Hospital has been using the multifocal IOL since April 2018, and this lens can provide an improvement in visual function that was not possible with the monofocal IOL and has considerably improved the degree of patient satisfaction. Femtosecond laser surgery can be performed without the use of knives and needles and can be considered as a precise and safe surgical procedure, and thus as a future standard surgical procedure for cataracts.

Key words: cataract surgery, multifocal IOL, quality of vision

Research on Infant-Sucking Behavior
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The feeding behaviors at either the breast or the bottle are based on peristaltic tongue movements. Nevertheless, many significant differences in feeding behaviors exist between the two feeding methods, including:

1) Elongation of nipple: artificial nipples are less elongated than human nipples.

2) Sucking patterns: breastfeeding results in a short-and-frequent sucking pattern with larger perioral muscle activity as compared to that of bottle-feeding.

3) The amount of milk: artificial nipples result in larger milk flow than human nipples.

4) Patterns of sucking pressure before and after milk ejection: during breastfeeding, infants exhibit the “call up” sucking behavior prior to the milk ejection reflex. On the contrary, milk flow is immediate when infants suck artificial nipples.

5) The jaw and throat movements during feeding: the jaw and throat movements are larger during bottle-feeding as compared to breastfeeding.

6) Coordination between suck-swallow-respiration: breastfeeding is a safer method for infants - it results in a lower drop in respiratory rate and tidal volume as compared to bottle-feeding.

When researching infants’ olfactory learning, I found that the odor of mother’s own milk alters infants’ sucking patterns after a 2-week separation from their mothers. This reaction to mother’s own milk may be explained by a genetically-acquired olfactory preference.

Key words: sucking behavior, breastfeeding, bottle-feeding

Original Sessions

1. The Relationship between Thyroid Function and CBF in Mild Cognitive Impairment and Alzheimer’s Disease
Shohei Nomoto1,2, Ryuta Kinno1, Hirota Ochiai2, Satomi Kubota1, Yukiko Mori1, Akinori Futamura1, Azusa Sugimoto1, Takeshi Kuroda1, Satoshi Yano1, Hidetomo Murakami1, Takako Shirasawa2, Takahiko Yoshimoto2, Akira Minoura2, Akatsuki Kokaze2, Kenjiro Ono3

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The thyroid hormones have been associated with cognitive decline and Alzheimer’s disease (AD), with a recent study linking thyroid function within the normal range and cerebral blood flow (CBF) in AD patients. Mild cognitive impairment (MCI) is often the first stage of AD, thus early diagnosis is important. The present study investigated the relationship between thyroid function and regional CBF (rCBF) in patients with MCI and AD. A total of 122 memory clinic outpatients who underwent thyroid function testing and single photon emission computed tomography were divided into MCI, AD, and Normal groups. RCBF was calculated using a three-dimensional stereotactic region-of-interest template in an automated cerebral perfusion single photon emission computed tomography analysis system. Multiple regression analysis adjusted for age
and sex was conducted to examine the relationships between thyroid hormones and rCBF. Thyroid stimulating hormone was significantly associated with rCBF in the bilateral temporal, bilateral pericallosal, and bilateral hippocampus regions in the MCI group. In the AD group, free triiodothyronine was significantly associated with rCBF in the bilateral parietal, right temporal, and bilateral pericallosal regions. The present study associated rCBF with thyroid stimulating hormone levels in a group of patients with MCI group, but with free triiodothyronine in AD patients. These study findings might inform the early diagnosis of MCI at general memory clinics and the prevention of subsequent progression to AD.

Key words: Alzheimer’s disease (AD), mild cognitive impairment (MCI), regional cerebral blood flow (rCBF), thyroid function, single photon emission computed tomography (SPECT)

2. Exchange of 519 Urethane Foam Mattresses at One Time Decreased the Hospital-acquired Pressure Ulcer Rate

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Introduction

Our hospital replaced 519 mattresses in use for more than 10 years at one time, enabling us to analyze the relationship between a patient’s mattress and the occurrence of hospital-acquired pressure ulcers.

Method

Our survey period was 3 years before and 5 years after the exchange of 519 mattresses in September 2012.

Analysis

We compared the occurrence of hospital-acquired pressure ulcers for 1 year before and after the exchange, and calculated a 1-year rate.

Results

The rate of hospital-acquired pressure ulcers was significantly different before and after the mattress exchange (1.10% vs. 0.74%; chi-square test, \( P < 0.05 \)). The yearly rates for hospital-acquired pressure ulcers before the mattress exchange were 1.39% (2010), and 1.49% (2011), and 1.64% (2012), compared to 0.69% (2013), 0.33% (2014), 0.38% (2015), 0.34% (2016), and 0.47% (2017) after the exchange. The rate thus increased for 3 years prior to the exchange of mattresses, and decreased directly after the exchange.

Discussion

Hospital-acquired pressure ulcers rate significantly decreased following the routine exchange of 519 mattresses. As a pressure-redistributing mattress, a urethane form mattress is useful for pressure ulcer prevention by the function of “immersion” and “envelopment”. In turn, mattress degradation causes “fatigue”, and a periodic exchange is recommended. Our research reaffirmed the importance of the mattress in pressure ulcer prevention.

Key words: urethane foam mattress, pressure-redistributing mattress, hospital-acquired pressure ulcers, mattress exchange of all hospital beds, mattress fatigue

3. Study of Gut Microbiota for Biomarker Detection in Patients with Kidney Cancer and Urothelial Cancer

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Many recent studies have demonstrated a relationship between gut microbiota and disease. In this study, we collected feces from patients with kidney or urothelial cancer to ascertain whether the composition of their gut microbiota affected metastasis and cancer type. We also looked for differences in the microbiota compositions...
depending on the neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR). NLR and PLR can reflect a patient’s inflammatory response and immune status, and is used as a prognostic predictor in various cancer types. From April 2018 to September 2018, we enrolled 54 patients in Showa University hospital for the present study. We analyzed the gut microbiota in all patients using 16S ribosomal RNA gene analysis by next-generation sequencing. We found a significant difference between Clostridiaceae and Verrucomicrobiaceae prevalence between patients with kidney and urothelial cancer. In addition, Peptostreptococcaceae was significantly greater in the absence of metastasis of urothelial carcinoma, and there was a significant difference between Rikenellaceae and Veillonellaceae when comparing patients with PLR ≥ 210 and PLR < 210. The diversity of intestinal bacteria was also poor in cases of metastatic kidney and urothelial cancer compared to patients with non-metastatic disease. In summary, our results revealed differences in gut microbiota between patients with different cancer types and between metastatic and non-metastatic cancer cases. Gut microbiota might therefore be useful in disease prevention, treatment targeting, and in predicting drug effects. Further accumulation of research is necessary.

Key words: gut microbiota, kidney cancer, urothelial cancer, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio

4. Bipedicled Mini V-Y Advancement Flap for Skin Defects of the Face

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Excision of facial skin tumors frequently leaves circular defects. These are primarily closed using dog-ear resection and direct approximation, resulting theoretically in scars up to three times the length of the original lesion. In young patients, even small circular facial defects after the excision of benign skin tumors present a reconstructive challenge, and the usefulness of a V-Y advancement flap for reconstructing such defects is well documented. We refined this technique as a mini V-Y advancement flap consisting of two subcutaneous pedicles that vascularize the skin island via subdermal plexus lateral bridges. The principle of the technique is to preserve a triangular skin that could be sacrificed when a circular skin defect is primarily closed, and to use it as a local flap. Unlike the conventional V-Y advancement flap, the skin island is vascularized via subdermal plexus lateral bridges of the two subcutaneous pedicles. Because the horizontally (subdermal plexus-based) bipedicled V-Y advancement flap moves only horizontally and is provided with stable blood supply, we believe that this procedure is superior to conventional, vertically (perforating vessel-based) pedicled V-Y advancement. This technique was used for 21 middle-aged or younger patients with a small benign skin lesion. None of them experienced any postoperative complications. Aesthetically excellent results were found in all patients. This small advancement flap could be attempted as an alternative to fusiform excision of small skin lesions, particularly in younger patients.

Key words: facial skin tumor, skin defect, advancement flap, subdermal plexus

5. The Relationship between Changes in Posterior Condylar Offset and Differences in Condylar Length and Range of Motion in Total Knee Arthroplasty

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2) Department of Orthopedic Surgery, Showa University Koto Toyosu Hospital

Purpose
This study investigated how pre- to postoperative changes in posterior condylar offset (PCO) relate to different condylar lengths and ranges of motion in posterior stabilized (PS) type total knee arthroplasty (TKA).

Materials and methods
We analyzed 40 knees of 40 patients (10 males and 30 females) treated with PS type TKA. Lengths of both condyles were measured intraoperatively by slide
calipers, and PCO was measured using plain X-ray. The patients were divided into two groups based on a pre-to postoperative change in PCO of ≥ 3 mm and < 3 mm. The differences in condylar length and range of motion were compared between the groups.

**Results**

The mean differences in condyle lengths were 2.6 mm (n = 33 knees) and 4.3 mm (7 knees) in cases with PCO changes of < 3 mm and ≥ 3 mm, respectively. The means in the respective groups were −6° and −7° for preoperative extension, 116° and 118° for preoperative flexion, −3° and −4° for postoperative extension, and 131° and 129° for postoperative flexion. There was no significant difference in ranges of motion between the groups.

**Discussion**

PS type TKA cases with a large difference in condyle lengths are likely to have a small PCO postoperatively, although postoperative knee range of flexion was not significantly related to a small postoperative PCO in this study. These findings suggest that preoperative range of knee motion, age, and type of TKA may influence both the postoperative range of knee motion and the PCO.

**Key words**: posterior condylar offset, range of motion, length of femoral condyle

6. **Distance between the Falciform Ligament and Distal Dural Ring as a Surgical Landmark for the Treatment of Paracclinoid Aneurysms**

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**Objective**

It is difficult to completely comprehend the anatomy of structures surrounding the paracclinoid region before an aneurysm or tumor treatment thereabouts; however, it is important to determine whether a paracclinoid aneurysm is intradural or extradural. Thus, accurate prediction of the distal dural ring (DDR) position is necessary. To this end, we focused on the falciform ligament (FL), which is easily visualized on images based on its anatomical features, and measured the distance between the FL and the DDR in patients undergoing paracclinoid-aneurysm operations.

**Methods**

From January 2017 to July 2018, we retrospectively identified 15 patients who underwent clipping to treat a paracclinoid-aneurysm. The distance between the FL and DDR was measured in all patients during surgery.

**Results**

The study group comprised 14 women and 1 man. The mean aneurysm diameter was 7.29 ± 2.21 mm, with a median of 6.5 mm. Eleven of the aneurysms were on the left and four were on the right side. The mean distance between the FL and the DDR was 3.50 ± 0.17 mm, with a median of 3.50 mm, thus showing little difference among the patients.

**Conclusions**

The position of the FL can be easily predicted using preoperative three-dimensional computed tomography angiography based on its anatomical features. In this study, the DDR was located 3.5 mm proximal to the FL along the internal carotid artery, providing useful data for predicting the position of the DDR.

**Key words**: 3D-CT angiography, distal dural ring, falciform ligament, paracclinoid aneurysms

7. **Safety and Curability of Laparoscopic Gastrectomy in Elderly Patients with Gastric Cancer**

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**Background**

Elderly patients are often considered as a high-risk population for major abdominal surgery due to reduced functional reserve and increased comorbidities. This study therefore assessed the safety and curability of laparoscopic gastrectomy in elderly patients with gastric cancer compared with short- and long-term outcomes in non-elderly patients.
**Methods**

We retrospectively investigated 386 patients who underwent laparoscopic gastrectomy for gastric cancer from January 2007 to December 2015 at the Digestive Disease Center, Showa University, Northern Yokohama Hospital. We categorized the patients into elderly (≥ 75 years old) and non-elderly (< 74 years old) groups. Patient characteristics, clinicopathologic and operative findings, and short- and long-term outcomes were investigated and compared between the groups.

**Results**

The elderly group showed a significantly higher rate of comorbidities (73.1% vs. 49.2%, P < 0.001) and American Society of Anesthesiologists (ASA) scores ≥ 2 (76.3% vs. 43.7%, P < 0.001). The postoperative morbidity and mortality did not differ between the groups (19.4% vs. 18.8%; P = 0.880, 2.2% vs. 0%; P = 0.058). The 5-year overall survival ratio was significantly lower in the elderly group than in the non-elderly group (67.7% vs. 85.0%; P < 0.001); however, the 5-year disease-specific survival ratio was similar across the groups (84.8% vs. 89.1%; P = 0.071).

**Conclusion**

Laparoscopic gastrectomy for gastric cancer could be safely performed in elderly patients with acceptable postoperative morbidity and curability.

**Key words**: laparoscopic gastrectomy, elderly patients, gastric cancer

8. **Submucous Cleft Palate and Congenital Velopharyngeal Inefficiency with Surgical Treatment of 22q11.2 Deletion Syndrome in our Hospital**

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The 22q11.2 deletion syndrome is a congenital disorder associated with palate abnormalities, congenital heart disease, distinctive facial features, developmental delay, and a variety of other congenital abnormalities. Submucous cleft palate (SMCP) and congenital velopharyngeal inefficiency (CVPI) are more common palate abnormalities than cleft palates. Herein, we compared velopharyngeal closure (VPC) between a 22q11.2 deletion syndrome group (22q group) and a non-22q11.2 deletion group (control group) and investigated treatment methods.

Subjects comprised 21 patients in the 22q group (7 cases of SMPC, 14 cases of CVPI), and 20 patients in the control group (9 cases of SMPC, 11 cases of CVPI) who presented to our hospital with a chief complaint of inarticulate speech and were available for spoken language evaluation. Cleft palate verbal examination, lateral cephalogram, and fiberscope were used to examine nasopharyngeal form and function, and rhinolalia aperta before and after surgery were compared to investigate treatments.

Palates were shorter and pharyngeal cavities were deeper in the 22q group than in the non-22q group, but there were no clear differences in palate movement.

A short palate and deep pharynx are believed to impact rhinolalia aperta. Cephalograms revealed no apparent differences in palate movements, but decreases in motion endurance may have resulted from decreased muscle tone. Pharyngeal flap surgery was primarily conducted in patients with CVPI, while SMCP patients were treated by Furlow’s technique or the pushback technique for bundle formation. In addition, if rhinolalia aperta is of moderate or higher severity, pharyngeal flap surgery should be considered.

**Key words**: 22q11.2 deletion syndrome, submucous cleft palate, congenital velopharyngeal inefficiency
9. Ultrasound-based Logistic Regression Modeling LR2 Versus Magnetic Resonance Imaging for Discriminating between Benign and Malignant Adnexal Masses

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Background

The diagnostic performances of the International Ovarian Tumor Analysis (IOTA) ultrasound-based logistic regression (LR2) model and magnetic resonance imaging (MRI) in discriminating between benign and malignant adnexal masses have not been directly compared in a single study.

Methods

Using the IOTA LR2 model and subjective interpretation of MRI findings by experienced radiologists, 265 consecutive patients with adnexal masses were preoperatively evaluated in two hospitals from February 2014 to December 2015. Definitive histological diagnosis of excised tissues was used as a gold standard.

Results

From the 265 study subjects, 54 (20.4%) tumors were histologically diagnosed as malignant (including 11 borderline and 3 metastatic tumors). Preoperative diagnoses of malignant tumors showed 91.7% total agreement between IOTA LR2 and MRI, with a kappa value of 0.77 (95% confidence interval [CI]: 0.68-0.86). The sensitivity of IOTA LR2 (0.94, 95% CI: 0.85-0.98) for predicting malignant tumors was similar to that of MRI (0.96, 95% CI: 0.87-0.99; P = 0.99), while the specific gravity of IOTA LR2 (0.98, 95% CI: 0.95-0.99) was significantly higher than that of MRI (0.91, 95% CI: 0.87-0.95; P = 0.002). Combining the IOTA LR2 and MRI results gave the greatest sensitivity (100, 95% CI: 0.93-1.00) and similar specificity to MRI (0.91, 95% CI 0.86-0.94).

Conclusions

The IOTA LR2 model had a similar sensitivity to MRI for discriminating between benign and malignant tumors and a higher specificity compared with MRI. Our findings suggest that that IOTA LR2 model, either alone or in conjunction with MRI, should be included in preoperative evaluation of adnexal masses.

Key words: IOTA, ultrasound, magnetic resonance imaging (MRI), ovarian tumor

10. Diagnostic Accuracy of Demarcation Using Magnifying Endoscopy with Narrow-Band Imaging for Helicobacter pylori-uninfected Undifferentiated-type Early Gastric Cancer

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Background

It is unknown how the accuracy rate of diagnostic demarcation of undifferentiated-type early gastric cancers differs between patients uninfected with Helicobacter pylori (H. pylori) and patients with and without H. pylori eradication. This study assessed and compared the diagnostic accuracy rate in the H. pylori-uninfected group and the non-H. pylori eradication and H. pylori eradication groups.

Methods

Subjects were 81 patients with 81 lesions who underwent endoscopic submucosal dissection (ESD) from January 2010 to January 2015. There were 21 lesions in the H. pylori-uninfected group, 27 in the H. pylori eradication group, and 33 in the non-H. pylori eradication group. The rate in the H. pylori-uninfected group was compared with the rates in the non-H. pylori eradication and H. pylori eradication groups.

Results

The diagnostic accuracy rates were 60.6% in the
non-\textit{H. pylori} eradication group, 92.2\% in the \textit{H. pylori} eradication group, and 100\% in the \textit{H. pylori}-uninfected group, showing a significantly higher rate in the \textit{H. pylori}-uninfected group than in the non-\textit{H. pylori} eradication group, but no significant difference between the \textit{H. pylori}-uninfected and \textit{H. pylori} eradication groups. In addition, the \textit{H. pylori}-uninfected and \textit{H. pylori} eradication groups showed no significant differences in neutrophil infiltration and intestinal metaplasia between them, whereas both were significantly milder in the \textit{H. pylori}-uninfected group.

\textbf{Conclusions}

Neutrophil infiltration was classified as mild or none, thus the accuracy of diagnostic demarcation was high in the \textit{H. pylori}-uninfected and \textit{H. pylori} eradication groups compared herein.

\textbf{Key words} : gastric cancer, endoscopic resection, \textit{Helicobacter pylori}, endoscopic gastrointestinal surgery

\section*{11. Diagnostic Examination of Acute Psychosis in a Super Emergency Ward —Comparison with Schizophrenia and Usefulness of Atypical Psychosis Diagnosis—}

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Karasuyama Hospital is an acute-care psychiatric hospital of Showa University that has two so-called super emergency wards, and charges a special admission fee for accepting psychiatric emergency patients. Due to difficulties obtaining detailed information of patient backgrounds and clinical history on presentation, an initial diagnosis of acute transient psychotic disorder remains unchanged until discharge in many cases. Although such a diagnosis is commonly given and clinically useful to some extent in psychiatric emergency practice, the clinical features of acute transient psychotic disorder remain undefined and hence are not often subjected to academic studies. We have created a database of patients admitted to the super emergency wards of our hospital between January 1, 2010 and December 31, 2014 by reviewing medical charts. Consistent with previous findings, the most common group of patients admitted to super emergency wards had schizophrenia, although 28 patients were diagnosed with acute transient psychotic disorder at the point of their discharge according to ICD-10IBH: please define this term and review this whole sentence to check that the intended meaning has been retained. In comparison to the 996 patients diagnosed with schizophrenia, the acute transient psychotic disorder patients tended to show drastic symptoms that cleared in a relatively short period of time following a small dose of major tranquilizers. Moreover, almost half of the cases diagnosed with acute transient psychotic disorder also met the diagnostic criteria of atypical psychosis. Based on our hospital findings, we suggest that the disease concept of atypical psychosis is important in psychiatric emergency patients diagnosed with acute transient psychotic disorder.

\textbf{Key words} : diagnosis, psychiatric emergency unit, acute psychosis, atypical psychosis, pharmacotherapy

\section*{12. The Clinical Impact of MRI Screening for BRCA Mutation Carriers: The First Report in Japan}

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\textbf{Background}

There is no consensus on the appropriate surveillance
for high-risk women with breast cancer in Japan. We therefore investigated their imaging features and pathological characteristics to build a proper surveillance system for asymptomatic high-risk individuals in the future.

**Methods**

We retrospectively reviewed 93 female BRCA1 and BRCA2 mutation carriers from our institutional clinical database from 2011 to 2017. The study population was composed of 112 breast cancers. Mammography and MRI were reviewed by examiners blinded to the patients’ clinical history. Final surgical or biopsy histopathology served as the reference standard in all patients.

**Results**

Of the 112 breast cancers reviewed, 59 breast cancers met selection criteria; of these, 30 were BRCA1 associated tumors, and 29 were BRCA2 associated tumors. Invasive ductal carcinoma was the most prevalent type in both BRCA1 and BRCA2. There were statistically significant differences in subtype, nuclear grade, and Ki-67 labeling index between BRCA1 and BRCA2 mutation carriers. Additionally, imaging findings on mammography and MRI were statistically different. Tumors in BRCA2 carriers demonstrated mammographic calcifications more frequently, while those in BRCA1 carriers more frequently demonstrated a mass or architectural distortion ($P < 0.001$). Enhancement patterns on MRI also significantly differed between the two subgroups ($P = 0.006$). The size of MRI-detected lesions was statistically smaller than the size of those detected by other modalities ($P = 0.004$).

**Conclusions**

The imaging and histological characteristics of BRCA1/2 mutation carriers were consistent with studies from other countries. MRI-detected lesions were significantly smaller than lesions detected by non-MRI modality and all lesions in BRCA1 mutation carriers could be detected by MRI.  

**Key words**: BRCA, high-risk patients, familial breast cancer, MRI surveillance, mammography

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**13. Relationship Between Islet Autoantibodies and Pancreatic Volume in Type 1 Diabetes in a Japanese Population**

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**Aims**

Our group previously reported that patients with type 1 diabetes (T1D) had significantly lower pancreatic size than non-diabetic controls (non-DCs). In the present study we investigated the relationship between pancreas size and titers of islet autoantibodies in acute-onset T1D and slowly progressive insulin-dependent diabetes mellitus (SPIDDM).

**Materials and methods**

The pancreatic volume (PV) was measured by computed tomography in 71 patients with T1D (32 acute-onset T1D and 39 SPIDDM) and 39 age- and body mass index-matched non-DCs. Autoantibody titers against glutamic decarboxylase-65 (GADAb), insulinoma-associated antigen-2 (IA-2Ab), and zinc transporter 8 (ZnT8Ab) were measured.

**Results**

The PV was significantly correlated with body weight in both T1D patients and non-DCs. The PV index (PVI; PV/body weight) was decreased by 40% in T1D compared with that in non-DCs, and PVI in SPIDDM reduced as the duration of diabetes progressed. No statistically significant correlation was found between the PVI and titers of GADAb and ZnT8Ab in acute-onset T1D and SPIDDM. Among the patients with T1D, PVI values were significantly lower in patients with high titers of IA-2Ab (≥10 U/ml) compared to those negative for IA-2Ab. The high IA-2Ab group had a high prevalence of acute-onset cases and high titers of GADAb and ZnT8Ab.

**Conclusions**

High titers of IA-2Ab reflect reduced pancreatic size in T1D patients, especially those with acute-onset
disease. The potential mechanisms underlying reduced pancreatic size might differ between acute-onset T1D and SPIDDM.

**Key words:** pancreatic volume, type 1 diabetes, islet-autoantibodies

**14. Seven Day Bounce-back Admission after Emergency Department Discharge in Japan**

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**Aims**

Unscheduled admissions after discharge from the emergency department (ED) (bounce-back admissions, BBAs) are monitored as a hospital performance measure in countries other than Japan. Whether BBAs reflect the quality of emergency care remains unclear; however, they might also be caused by diagnostic errors. This study aimed to determine the frequency of 7- and 3-day BBAs (7d-BBAs and 3d-BBAs) in a tertiary medical institution in Japan.

**Methods**

Retrospective analysis was conducted in adult (18 years) patients who visited the ED of Showa University Hospital from June 2011 to May 2013 (n = 15,069). Patients with index ED visits were registered and followed up for unscheduled admissions to this hospital within 3 and 7 days. Diagnoses upon discharge and admission of 7d-BBA cases were compared.

**Results**

Among the 11,669 patients discharged according to physicians’ order, 180 had 3d-BBAs and 257 had 7d-BBAs. Among the 7d-BBA cases, 117 had similar and 110 had different discharge and admitting diagnoses; for the remaining 30 cases, the results could not be ascertained owing to incomplete diagnostic data.

**Conclusions**

The frequency of 7d-BBA and 3d-BBA in this study was similar to the results in previous studies conducted with the same definition of unplanned admission. Analyzing the discharge and admitting diagnoses may promote reduction of BBAs. Further multicentric studies are necessary to determine the ideal level of BBAs in Japan.

**Key words:** unplanned admission, misdiagnosis, mistreatment

**15. High Expression of Olfactomedin-4 is Correlated with Chemoresistance and Poor Prognosis in Pancreatic Cancer**

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**Purpose**

Pancreatic cancer has an extremely poor prognosis, and identification of novel predictors of therapeutic efficacy and prognosis is urgently needed. Chemoresistance-related molecules are correlated with poor prognosis and may be effective targets for cancer treatment. Here, we aimed to identify novel molecules correlated with chemoresistance and poor prognosis in pancreatic cancer.

**Experimental design**

We established 10 patient-derived xenograft (PDX)
lines from patients with pancreatic cancer and performed next-generation sequencing (NGS) of tumor tissues from these xenografts after treatment with anticancer drugs. We established a gene-transferred tumor cell line to express chemoresistance-related molecules and analyzed the chemoresistance of the established cell line against anticancer drugs. Finally, we performed immunohistochemical (IHC) analysis of chemoresistance-related molecules using 80 pancreatic cancer tissues.

**Results**

From NGS analysis, we identified olfactomedin-4 (OLFM4) as highly expressed in the PDX group treated with anticancer drugs. By IHC analysis, OLFM4 expression was also high in PDXs administered anticancer drugs compared with untreated PDXs. Chemoresistance was observed by in vitro analysis using tumor cell lines with forced expression of OLFM4, and in Kaplan-Meier analysis of tissue specimens from 80 patients with pancreatic cancer, the low OLFM4 expression group had a better survival rate than the high OLFM4 expression group. Additionally, multivariate analysis showed that high expression of OLFM4 was an independent prognostic factor predicting poor outcomes.

**Conclusions**

High expression of OLFM4 was involved in chemoresistance and was an independent prognostic factor in pancreatic cancer. OLFM4 may be a candidate therapeutic target in pancreatic cancer.

**Key words:** olfactomedin-4, pancreatic cancer, chemoresistance, prognosis, biomarker

16. withdrawal

17. Clinical Characteristics and Prognostic Factors of Pneumonia in Patients with and without Rheumatoid Arthritis

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Pneumonia is associated with increased mortality in rheumatoid arthritis (RA) patients; however, no reported studies have investigated the etiology of pneumonia in RA patients. We thus assessed whether pneumonia in RA patients differs from that in non-RA patients.

We retrospectively divided pneumonia patients into two groups, those with RA and those without RA, and compared the two groups. We evaluated the risk factors for mortality by univariate and multivariate logistic regression analysis.

Among 1549 patients, 71 had RA. The RA patients with pneumonia were 71.0 ± 8.9 years old, 54.9% were female, 40.9% had a smoking history, and 71.8% had underlying respiratory disease. Female gender, non-smoker, and respiratory comorbidities were statistically more frequent in RA patients than non-RA patients. The most frequent causative microbial agents of pneumonia in RA patients were _Streptococcus pneumoniae, Pseudomonas aeruginosa, and Haemophilus influenzae_, whereas those of pneumonia in non-RA patients were _Streptococcus pneumoniae_, _influenza virus_, and _Mycoplasma pneumoniae_. _Pseudomonas aeruginosa, Haemophilus influenzae, Moraxella catarrhalis_, and polymicrobial infection were identified as etiologies more frequently found in RA patients than non-RA patients. Although the severity of pneumonia did not differ between the groups, mortality was statistically higher in RA patients than non-RA patients. Multivariate analysis showed RA to be an independent risk factor for mortality.

Our findings suggest that _Pseudomonas aeruginosa, Haemophilus influenzae, Moraxella catarrhalis_, and polymicrobial infection were statistically more frequent etiologies of pneumonia in RA patients than non-RA patients. RA itself was found to be an independent risk factor for mortality from pneumonia.

**Key words:** rheumatoid arthritis, pneumonia, etiology, mortality, prognostic factor
18. Etelecalcetide for Managing Secondary Hyperparathyroidism in Hemodialysis Patients
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Background
We retrospectively assessed the usefulness of a new calcimimetic, etelcalcetide, in Japanese chronic hemodialysis patients with secondary hyperparathyroidism. The aim of this study was to assess the therapeutic reactivity of etelcalcetide.

Methods
The participants were 43 patients (average age, 60 years; average dialysis period, 90.7 months) with serum intact parathyroid hormone (iPTH) levels ≥ 240 pg/ml. Intravenous injection of etelcalcetide was started at 15 mg/week for 12 weeks and the dose was adjusted to control the serum levels of iPTH, corrected calcium (cCa), and phosphorus (P).

Results
In total, 81.3% of patients had a reduction of iPTH of ≥ 50% at 12 weeks, and 32% achieved the target levels for P, cCa, and PTH. In multivariate analysis, female sex and a history of cinacalcet administration were independent inhibitory factors for iPTH reduction. Compared to patients with a history of cinacalcet administration (n = 22), those without this history (n = 21) had a higher rate of a ≥ 50% reduction in iPTH (63.6% vs. 95.2%, respectively; P = 0.007) and of achieving target levels for P, cCa, and iPTH (22.7% vs. 42.9%, respectively; P = 0.15). The side effects of the patients during the observation period were hypocalcemia (44%), nausea (7%), and muscle spasms (2.3%).

Conclusions
Our results show that etelcalcetide can improve management of iPTH together with cCa and P levels in Japanese hemodialysis patients with secondary hyperparathyroidism. There is a tendency for iPTH levels to slowly decrease in patients with a history of cinacalcet administration.

Key words: etelcalcetide, cinacalcet, calcimimetics, secondary hyperparathyroidism, hemodialysis

19. Current Pharmacotherapy of Patients with Bipolar Disorders at Psychiatric Emergency Wards at Showa University Karasuyama Hospital
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Although bipolar disorder is one of the most common psychiatric disorders, its pharmacotherapy is still not well established. In this study, we evaluated the current medication use of 221 individuals diagnosed with bipolar disorder according to the Diagnostic and Statistical Manual of Mental Disorders (fifth edition) criteria, who were admitted to psychiatric emergency wards at Showa University Karasuyama Hospital between January 2010 and December 2013. Data on sociodemographics, clinical characteristics, and medications at admission and discharge or the end of the study period were collected on all individuals admitted to the wards during the period by a retrospective chart review. In total, 1899 individuals were admitted to the emergency wards, of whom 440 had mood disorders and 221 of these were diagnosed with bipolar disorders. The mean age of the bipolar disorder-diagnosed patients was 51.1 years old, which was higher than that of total patients admitted to the emergency wards. For the medications at admission, 132 (59.7%) were on mood-stabilizers, 169 (76.5%) were on anti-psychotics, and 79 (35.7%) were on anti-depressants. For the medications at discharge or the end of the study period, 166 (75.1%) were on mood-stabilizers, 184 (83.3%) were on anti-psychotics, and 54 (24.4%) were on anti-depressants. It was found that for individuals with bipolar disorders, the rate of co-administration of mood-stabilizers and anti-psychotics increased, and more anti-psychotics were used than mood-stabilizers during the period of admission at emergency wards. Further studies on the efficacy of medications in relation to clinical characteristics are planned.

Key words: bipolar disorder, pharmacotherapy, psychiatric emergency ward