| **Title:** | Optimal pressure for measuring objective lymphedema with postoperative ultrasonography in patients with breast cancer |
| **Author:** | Chaiyoung Lim, Byungkwan Hwang, Hee-Won Park, Do-Hong Lee, Ji-Eung Park, Kyu Jin Lee, Sun Kwon Kim & Kwan Sik Seo |
| **Journal:** | Computer Assisted Surgery Pages 1-9 | Published online: 27 Oct 2016 |
| **Abstract:** | **Objective:** To examine the reliability of ultrasonographic thickness and compressibility along with real-time pressure monitoring to evaluate postmastectomy lymphedema and to suggest a reference range of appropriate pressure.  
**Design:** Measurement reliability study.  
**Setting:** Research laboratory.  
**Participants:** Fifteen patients with prior mastectomy for breast cancer who were diagnosed with secondary lymphedema, and 16 healthy control subjects.  
**Methods:** The thickness and compressibility of the subcutaneous layer in the arms of 15 postmastectomy patients with secondary lymphedema were measured using B-mode and M-mode ultrasonography. An ultrasound machine was equipped with a real-time pressure-monitoring device to monitor downward compression pressure on the arms at a constant velocity. The ratio of thickness change defined the compressibility index. Two different experienced examiners participated in the measurement of lymphedema. Intrarater reliability and inter-rater reliability were estimated using the intraclass correlation coefficient. Very good reliability was defined as an ICC of more than 0.8.  
**Main outcome measurements:** The thickness of the subcutaneous layer, the compressibility index, and the intrarater and inter-rater reliability were measured.  
**Results:** The measured thicknesses demonstrated very good intrarater and inter-rater reliability for the forearm and upper arm. For the compressibility index, the
upper arm and forearm had very good intrarater and inter-rater reliability at over 2000 Pa of compression (>0.9).

**Conclusions**: Ultrasonography with real-time pressure monitoring may be useful for evaluating the severity and characteristics of lymphedema, particularly at compression pressures more than 2000 Pa.

**Database**: Taylor & Francis Online Journal

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**Title**: Evaluating environment radiations at Axesse linac undergoing NPC treatment of VMAT


**Journal**: Computer Assisted Surgery: Published online: 28 Oct 2016, Pages: 1-5 | DOI: 10.1080/24699322.2016.1240308

**Abstract**: Environment radiations in vault rooms resulting from Axesse linac use was assessed at Medical University Hospital using Thermoluminescent dosimeters (TLDs) during the use of the new radiation treatment known as volumetric modulated arc therapy (VMAT) in the treatment of nasopharyngeal cancer (NPC). The TLD-100H was calibrated using linac 6 MV photons. A total of 75 measurement points of the TLD-100H were utilized for environmental monitoring. The measured environment radiations were then visualized as three-dimensional graphical representations. Environment radiations were visualized using colored three-dimensional graphical representations. The radiations in NPC treatment of Rando phantom was found to reach levels up to 370 mSv/treatment. Many researchers consider TLD, which is the most cost-effective method to environment radiations. The minimum detectable dose (MDD) was also identified to demonstrate the reliability of the TLD approach. Quantitative results that provide practical guidance with regard to radiation protections. Potentially hazardous of secondary radiations from the operating linac is evaluated with regard to its potential health effects on both patients and the public.

**Database**: Taylor & Francis Online Journal
**Title:** Liposomal nano-drugs based on amphipathic weak acid steroid prodrugs for treatment of inflammatory diseases

**Author:** Keren Turjeman & Yechezkel Barenholz

**Journal:** Journal of Drug Targeting: Published online: 28 Oct 2016, Pages: 1-16 | DOI: 10.1080/1061186X.2016.1236262

**Abstract:**

**Background:** Steroids are the most efficacious anti-inflammatory agents. However, their toxicities and side-effects compromise their clinical application. Various strategies and major efforts were dedicated for formulating viable liposomal glucocorticosteroids (GCs), so far none of these were approved.

**Objectives:** To evaluate these approaches for formulating GC-delivery systems, especially liposomes, and with focus on the Barenholz Lab experience.

**Methods:** We developed PEGylated nano-liposomes (NSSL) remotely loaded with water-soluble amphipathic weak acid GC-prodrugs. Their remote loading results in high, efficient and stable loading to the level that enables human clinical use. We characterized them for their physical chemistry and stability. We demonstrated their therapeutic efficacy in relevant animal models and studied their pharmacokinetics (PK), biodistribution (BD) and pharmacodynamics advantages over the free pro-drugs.

**Results:** Our steroidal nano-drugs demonstrate much superior PK, BD, tolerability and therapeutic efficacies compared to the free pro-drugs and to most drugs currently used to treat these diseases. These nano-drugs act as robust immune-suppressors, affecting cytokines secretion and diminishing hemorrhage and edema.

**Conclusions:** The combination of improved physical-chemistry, PK, BD, tolerability and therapeutic efficacy of these steroidal nano-drugs over the pro-drugs “as-is” support their further clinical development as potential therapeutic agents for treating inflammatory diseases.

**Database:** Taylor & Francis Online Journal
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<th>Title</th>
<th>Attributable Risk of Infection to mTOR Inhibitors Everolimus and Temsirolimus in the Treatment of Cancer</th>
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<tr>
<td>Author</td>
<td>Christine A. Garcia &amp; Shenhong Wu</td>
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<td>Journal</td>
<td>Cancer Investigation: Published online: 28 Oct 2016, Pages: 1-10</td>
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<tr>
<td>Abstract</td>
<td>The risk of infection attributable to mTOR inhibitors has not been determined. Databases from PubMed and abstracts presented at the American Society of Clinical Oncology meetings were searched. Eligible studies included randomized controlled trials, in which everolimus or temsirolimus was compared with placebo. A total of 12 trials were included. The attributable incidences of all-grade and high-grade infections to mTOR inhibitors were 9.3% (95% confidence interval (CI): 5.8–14.6%) and 2.3% (95% CI: 1.2–4.4%) respectively. The risk varied widely with tumor types (p &lt;.001). There was substantial risk of infection attributable to mTOR inhibitors everolimus and temsirolimus.</td>
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<td>Taylor &amp; Francis Online Journal</td>
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<th>Title</th>
<th>Oral, frozen fecal microbiota transplant (FMT) capsules for recurrent Clostridium difficile infection</th>
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<tr>
<td>Author</td>
<td>Hamed Khalili, Joanne Levin, Jess L. Kaplan and Elizabeth L. Hohmann</td>
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<td>Abstract</td>
<td>Abstract</td>
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<td></td>
<td>Background</td>
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<td></td>
<td>Fecal microbiota transplantation (FMT) has been shown to be safe and effective in treating refractory or relapsing C. difficile infection (CDI), but its use has been limited by practical barriers. We recently reported a small preliminary feasibility study using orally administered frozen fecal capsules. Following these early results, we now report our clinical experience in a large cohort with structured follow-up.</td>
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<td>Methods</td>
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<td>We prospectively followed a cohort of patients with recurrent or refractory CDI who were treated with frozen, encapsulated FMT at our institution. The primary endpoint</td>
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was defined as clinical resolution whilst off antibiotics for CDI at 8 weeks after last capsule ingestion. Safety was defined as any FMT-related adverse event grade 2 or above.

**Results**

Overall, 180 patients aged 7–95 years with a minimal follow-up of 8 weeks were included in the analysis. CDI resolved in 82 % of patients after a single treatment, rising to a 91 % cure rate with two treatments. Three adverse events Grade 2 or above, deemed related or possibly related to FMT, were observed.

**Conclusions**

We confirm the effectiveness and safety of oral administration of frozen encapsulated fecal material, prepared from unrelated donors, in treating recurrent CDI. Randomized studies and FMT registries are still needed to ascertain long-term safety.

### Database

**Title:** Physician agreement regarding the expansion of pharmacist professional activities in the management of patients with asthma

**Author:** Audrey Tilly-Gratton, Alexandrine Lamontagne, Lucie Blais, Simon L. Bacon, Pierre Ernst, Roland Grad, Kim L. Lavoie, Martha L. McKinney, Eve Desplats and Francine M. Ducharme

**Journal:** International Journal of Pharmacy Practice: Version of Record online: 24 OCT 2016 | DOI: 10.1111/ijpp.12320

**Abstract**

**Background**

Asthma control remains suboptimal in Canada. Expansion of pharmacist's professional activities offers the opportunity to improve the interdisciplinary management of patients with asthma.

**Objective**

The aim of this study was to determine the level of agreement of physicians regarding the expansion of pharmacists' professional activities in the management of asthma patients.

**Methods**
We conducted a survey of randomly selected Quebec physicians in family medicine, paediatrics and emergency medicine. A 102-item questionnaire, including 10 questions regarding pharmacist's expanded professional activities, was sent using the Tailored Design Method. Questions were answered on a 6-point Likert-like scale (0 — strong disagreement to 5 — strong agreement).

**Results**

With a 56% response rate, 421 (250 family medicine, 115 paediatric and 56 emergency medicine) physicians participated; the median years of practice (25%, 75%) was 13 (5–21) years and 69% of respondents were women. Physicians were in favour of the expansion of pharmacist's professional activities with strong endorsement rates (rating of ≥4 on a maximum of 5) exceeding 60% for all but three activities: suggesting a written action plan to the physician (55%), adjusting the dose of prescribed asthma medication to achieve a therapeutic target (52%) and offering spirometry testing in pharmacies (45%). Emergency physicians, physicians with fewer years of practice, and those with a favourable perception of an interprofessional approach were associated with higher endorsement of these activities.

**Conclusion**

Physicians are favourable to the expansion of pharmacist activities in the management of patients with asthma. More complex activities were less frequently endorsed. The characteristics of strong intenders have been identified.

**Database** : Wiley Online Library

**Title** : Pathophysiology of the Desmo-Adhesome

**Author** : Antonio Celentano, Michele Davide Mignogna, Michael McCullough and Nicola Cirillo

**Journal** : Journal of Cellular Physiology: Version of Record online: 27 OCT 2016 | DOI: 10.1002/jcp.25515

**Abstract** : Advances in our understanding of desmosomal diseases have provided a clear demonstration of the key role played by desmosomes in tissue and organ physiology, highlighting the importance of their dynamic and finely regulated structure. In this context, non-desmosomal regulatory molecules have acquired
increasing relevance in the study of this organelle resulting in extending the desmosomal interactome, named the “desmo-adhesome.” Spatiotemporal changes in the expression and regulation of the desmo-adhesome underlie a number of genetic, infectious, autoimmune, and malignant conditions. The aim of the present article was to examine the structural and functional relationship of the desmosome, by providing a comprehensive, yet focused overview of the constituents targeted in human disease. The inclusion of the novel regulatory network in the desmo-adhesome pathophysiology opens new avenues to a deeper understanding of desmosomal diseases, potentially unveiling pathogenic mechanisms waiting to be explored.

Database: Wiley Online Library

Title: Forecasting oral absorption across biopharmaceutics classification system classes with physiologically based pharmacokinetic models

Author: Simone Hansmann, Adam Darwich, Alison Margolskee, Leon Aarons and Jennifer Dressman

Journal: Journal of Pharmacy and Pharmacology: Version of Record online: 26 OCT 2016 | DOI: 10.1111/jphp.12618

Abstract: Objectives
The aim of this study was (1) to determine how closely physiologically based pharmacokinetic (PBPK) models can predict oral bioavailability using a priori knowledge of drug-specific properties and (2) to examine the influence of the biopharmaceutics classification system class on the simulation success.

Methods
Simcyp Simulator, GastroPlus™ and GI-Sim were used. Compounds with published Biowaiver monographs (bisoprolol (BCS I), nifedipine (BCS II), cimetidine (BCS III), furosemide (BCS IV)) were selected to ensure availability of accurate and reproducible data for all required parameters. Simulation success was evaluated with the average fold error (AFE) and absolute average fold error (AAFE). Parameter sensitivity analysis (PSA) to selected parameters was performed.

Key findings
Plasma concentration–time profiles after intravenous administration were forecast within an AAFE < 3. The addition of absorption processes resulted in more variability in the prediction of the plasma profiles, irrespective of biopharmaceutics classification system (BCS) class. The reliability of literature permeability data was identified as a key issue in the accuracy of predicting oral drug absorption.

**Conclusion**

For the four drugs studied, it appears that the forecasting accuracy of the PBPK models is related to the BCS class (BCS I > BCS II, BCS III > BCS IV). These results will need to be verified with additional drugs.

**Database**

Wiley Online Library

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**Title**: Metastatic Patterns of Solitary Fibrous Tumors: A Single-Institution Experience

**Author**: Ailbhe C. O’Neill, et al.

**Journal**: American Journal of Roentgenology | Oct 20, 2016 | Ahead of Print

**Abstract**

**OBJECTIVE**: The objective of our study was to evaluate the metastatic patterns and imaging features of solitary fibrous tumors (SFTs).

**MATERIALS AND METHODS**: This retrospective study included 139 patients with pathologically proven SFT, 49 of whom developed metastases. Electronic medical records and all available images were reviewed to record the pattern and imaging appearances of metastatic disease, and comparisons of thoracic SFTs and extrathoracic SFTs were also performed. Associations of metastatic spread were studied using univariate and multivariate Cox regression analyses.

**RESULTS**: A total of 49 (35%) patients developed metastases at a median of 124 months (interquartile range [IQR], 66–195 months) after SFT diagnosis; 11 patients (8%) had metastases at presentation. Of these 49 patients, 40 patients died at a mean of 183 months after diagnosis. The associations with metastatic disease on univariate analysis were tumor size $\geq 10$ cm ($p = 0.01$) and malignant pathology or mitotic count $\geq 4$ per 10 high-power fields (HPF) ($p < 0.001$).

Malignant pathology and a mitotic count of $\geq 4$ per 10 HPF were also associated with metastatic disease on multivariate analysis ($p = 0.01$; hazard ratio, 0.22; 95% CI, 0.05–0.73). The most common sites of metastasis were the lungs (30/49, 61%).
followed by the pleura (24/49, 49%) and then the liver (20/49, 41%), bones (20/49, 41%), and peritoneum (20/49, 41%). A significantly higher proportion of patients with extrathoracic SFT had metastatic disease (37/139, 27%) compared with those with thoracic SFT (12/139, 9%) (p = 0.003). The overall metastasis-free survival was a median of 117 months (IQR, 33–169 months) in patients with extrathoracic SFT and a median of 120 months (IQR, 82–169 months) in patients with thoracic SFT (p = 0.01).

**CONCLUSION.** A mitotic count of ≥ 4 per 10 HPF or malignant pathology was significantly associated with metastatic disease on both univariate and multivariate analyses. The sites of metastatic disease differed depending on the site of the primary SFT but were most commonly the lung and pleura. Patients with extrathoracic SFT had a significantly higher proportion of metastatic disease compared to those with thoracic SFT.

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<th>Title</th>
<th>Real-Time 3D CT Image Guidance for Transjugular Intrahepatic Portosystemic Shunt Creation Using Preoperative CT: A Prospective Feasibility Study of 20 Patients</th>
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<tr>
<td>Author</td>
<td>Xuefeng Luo, Xiaoze Wang, Yin Zhao, Huaiyuan Ma, Linchao Ye, Li Yang, Jiaywei Tsauo, Mingshan Jiang and Xiao Li</td>
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<tr>
<td>Journal</td>
<td>American Journal of Roentgenology</td>
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</table>
| Abstract | **OBJECTIVE.** The purpose of this study is to prospectively evaluate the feasibility and efficacy of real-time 3D CT image guidance during transjugular intrahepatic portosystemic shunt (TIPS) creation.  

**SUBJECTS AND METHODS.** Between October 2013 and December 2013, a total of 20 patients were prospectively enrolled in the present study. Previously acquired portal venous phase CT datasets and intraoperative CT datasets were registered on a dedicated workstation. We accomplished semiautomatic registration for the datasets of 11 of 20 patients (55%), and we performed manual registration for the datasets of the remaining nine patients. The selected volume of interest of the CT image showing the portal vein vasculature was overlaid onto the fluoroscopic display to provide real-time 3D CT image guidance during the procedure. |
RESULTS. For all 20 patients, TIPS procedures were successfully performed by the same operator. The mean (± SD) number of needle passes required for portal vein entry was 1.8 ± 1.1 passes (range, 1–5 passes). The mean duration of radiographic fluoroscopy was 3.5 ± 1.1 minutes for portal vein entry and 11.4 ± 2.1 minutes for the whole procedure. The mean radiation dose used for the whole TIPS procedure was 295.5 ± 66.6 Gy · cm². No major technical complications were observed.

CONCLUSION. Real-time 3D guidance with the use of preoperative CT is feasible, safe, and effective for assisting in the creation of TIPS. This approach may result in a shorter procedural time and less radiation exposure. However, future studies are required to compare this method with other mapping techniques.

Database: American Roentgen Ray Society