

Program & Abstracts

4th Conference «Graubünden forscht – Young Scientists in Contest»
September 10–11, 2014 · Davos Congress Center, Entrance «Promenade Nord», Promenade 92, Davos, Switzerland

Guest institutions: alpS Innsbruck, European Academy of Bozen/Bolzano, Free University of Bozen/Bolzano



Academia Rætica gratefully acknowledges the support of the following institutions:



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Christine Kühne – Center for Allergy Research and Education



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Welcome

Academia Raetica welcomes you to the fourth conference «Graubünden forscht – Young Scientists in Contest». The conference is a showcase for research «made in Grisons», providing a great platform for young researchers to present their up-to-date research. In addition, the event enhances the academic exchange with the neighbouring regions: For the second time, alps from Innsbruck, Tyrol, and the European Academy of Research and Free University of Bozen, South Tyrol, will be taking part in our conference. Representatives from research and industry will debate the needs of young academics and the relational triangle between research, education, and innovation in the Grisons during two podium discussions.

The concluding highlight of the two-day conference will be the award ceremony of the newly founded Graduate School Graubünden (GSGR). With this event, Academia Raetica honors young researchers who have successfully completed their dissertation in 2013 and 2014. A Certificate of Merit will express our appreciation for their dedication to complete their degree in our alpine region.

To our great pleasure, the government of the Canton of Grisons has enacted the «Gesetz über Hochschulen und Forschung» (Law on higher education and research). The new law, which became operative on August 1, 2014, is the necessary foundation for the formation of the Graduate School Graubünden (GSGR), a support platform for doctoral and post-doctoral researchers. In cooperation with ETH and University of Zurich, the GSGR strengthens the existing connection between the Swiss universities and the Grisons-based research institutions. The law will enable the research institutions to apply for institutional funding from the Canton of Grisons and thus secure federal funding as well. This is a remarkable step for the Canton of Grisons.

We sincerely thank our participants, chairpersons, keynote and podium speakers, reviewers, staff and ultimately our sponsors for their support and effort.



Prof. Dr. med. Markus Furrer
President Academia Raetica

CK-CARE Allergy Education Week

CK-CARE, member institution of Academia Raetica, organizes the CK-CARE Allergy Education Week at the Davos Congress Center.

Education is CK-CARE's second pillar alongside research. Our goal is to translate the latest allergy research findings and to deliver knowledge updates to the fingertips of physicians of different specialties as well as other relevant health care providers who treat patients suffering from allergic diseases.

With the first CK-CARE Allergy Education Week in Davos from September 10–14, 2014 we want to contribute to a better patient management in the field of allergology by providing education that is learner-centered and based on real needs. We also want to encourage participants to engage in discussions, to exchange their personal experiences, to connect with each other, and generate new ideas from this.

There will be several parallel programs targeting a range of different medical professionals who are responsible for taking care of allergy sufferers. Alongside a 2-day CK-CARE Summer School focused on Eczema/Dermatitis we offer interactive seminars such as «Application of mindfulness in clinical practice» and workshops for our German-speaking community: «Basiswissen Anaphylaxie für Hausärzte und MPAs/MFAs in der Grundversorgerpraxis», «Motivierende Gesprächsführung» and «Schulung für Pflegefachkräfte – Therapie und Hautpflegeanleitung für Patienten mit Neurodermitis». Furthermore, the Train-the-Trainer programs enable to gain certification for patient trainers in anaphylaxis and atopic dermatitis.



Prof. Dr. med. Cezmi A. Akdis
Chairman Board of Directors CK-CARE

Program

Wednesday, September 10, 2014

09:30–10:00 Opening

Caviezel, Tarzisius	Mayor, Municipality of Davos	Forschung in Davos – Forschung für Davos
Jäger, Martin	Head, Department of Education, Culture and the Environment, Member of the Governing Council of the Canton of Grisons	Graubünden – ein Kanton mit Ambitionen
Furrer, Markus	President Academia Raetica	Eine Graduate School für Graubünden
Akdis, Cezmi	Director CK-CARE and Swiss Institute of Allergy and Asthma Research	Allergy Education Week

10:00–12:00 Oral Presentations: Medical Sciences

Fehr, Thomas	Kantonsspital Graubünden	Chair
Furrer, Markus	Academia Raetica	Chair
10:00–10:30 Alini, Mauro	AO Research Institute	Keynote: Present and future of tissue engineering
10:30–10:45 Wawrzyniak, Paulina	Swiss Institute of Allergy and Asthma Research	Epigenetic mechanisms for weaker expression of tight junctions in bronchial epithelial cells from asthmatic individuals 1
10:45–11:00 van de Veen, Willem	Swiss Institute of Allergy and Asthma Research	Generation and characterization of human allergen-specific B cell clones 2
11:00–11:15 Florio, Maria Cristina	EURAC research – Center for Biomedicine	Acetylation of SERCA2a: A new potential strategy to modulate calcium dynamics 3
11:15–11:30 Makwana, Priyanka	AO Research Institute	Effects of lipids and cholesterol on the chondrogenesis of human mesenchymal stem cells 4
11:30–11:45 Lang, Gernot	AO Research Institute	Biomimetic nucleus pulposus replacement for the treatment of degenerative disc disease 5
11:45–12:00 Sabaté Brescó, Marina	AO Research Institute	Assessing the role of implant stability on the development of staphylococcal osteomyelitis in a murine fracture model 6

12:00–13:30 Lunch and Poster Viewing

13:30–14:30 Oral Presentations: Humanities

Risi, Marius	Institut für Kulturforschung Graubünden	Chair
Zink, Albert	EURAC research – Institute for Mummies and the Iceman	Chair
13:30–13:45 Jecklin-Tischhauser, Ursina	Amt für Kultur Graubünden	Die Kirchenanlage Sogn Murezi in Tomils (GR) – kirchliches und herrschaftliches Zentrum im frühmittelalterlichen Churrätien 7
13:45–14:00 Paladin, Alice	EURAC research – Institute for Mummies and the Iceman	Scientific analysis of human remains: from the Egyptian mummy of the Natural History Museum of Venice-Italy, to the medieval skeletons of South Tyrol-Italy 8
14:00–14:15 Naef, Leandra	Institut für Kulturforschung Graubünden	*Altes Eis – Gletscherarchäologie in Graubünden 9
14:15–14:30 Coia, Valentina	EURAC research – Institute for Mummies and the Iceman	Demographic and cultural factors in shaping the genetic variation of alpine ethno-linguistic groups 10

14:30–16:00 Poster Presentations (P1–P14): Natural and Technical Sciences

Ammann, Walter	Global Risk Forum GRF Davos	Chair
Haller, Ruedi	Parc Naziunal Svizzer	Chair
Aebi, Christine	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	A comprehensive radiation flux assessment at different sites in Switzerland P1

Wednesday, September 10, 2014

	Chinellato, Giulia	EURAC research – Institute for Applied Remote Sensing	Remote and terrestrial ground monitoring techniques integration for hazard assessment in mountain areas	P2
	Cortines, Felipe	EURAC research – Institute for Alpine Environment	WIKIAlps: A wiki for capitalizing on spatial-development projects	P3
	Egorova, Tatiana	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	Solar variability and climate change during the first half of the 20th century (SOVAC)	P4
	Guerreiro, Nuno	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	The role of small scale heating events in the coronal heating	P5
	Köhler, Anselm	WSL Institute for Snow and Avalanche Research SLF	On the potential of a novel avalanche radar system	P6
	la Cour, Jakob Bonne	CSEM Landquart	Electrochemical microsensors for monitoring the functions of liver cells in a modular based microfluidic system	P7
	Schmid, Lino	WSL Institute for Snow and Avalanche Research SLF	Simulation of snow stratigraphy using full-wave form inversion applied to data from an upward-looking radar system	P8
	Steinkogler, Walter	WSL Institute for Snow and Avalanche Research SLF	Granulation of snow: Experiments and discrete element modeling	P9
	Suter, Markus	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	Measurements of the Total Solar Irradiance	P10
	Tagirov, Rinat	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	Fast non-LTE radiative transfer numerical scheme for solar spectrum modeling	P11
	Veitinger, Jochen	WSL Institute for Snow and Avalanche Research SLF	Modeling of winter terrain surface to improve avalanche release zone estimation	P12
	Walter, Benjamin	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	The «Monitor to measure the integral transmittance of windows» (MITRA)	P13
	Zgaga, Janez	Freie Universität Bozen	Vernetzungskonzepte für Smart Home Anwendungen mittels kostengünstiger Plattformlösungen und bestehender Standards	P14

16:00–16:30 Coffee Break
16:30–17:30 Oral Presentations: Natural and Technical Sciences

	Ammann, Walter Schweizer, Jürg	Global Risk Forum GRF Davos WSL Institute for Snow and Avalanche Research SLF	Chair Chair	
16:30–16:45	Schweiger, Anna	Parc Naziunal Svizzer	Spatial movement patterns and high-resolution remote sensing data explain resource selection of three sympatric ungulate species	11
16:45–17:00	Steinkogler, Walter	WSL Institute for Snow and Avalanche Research SLF	Linking snow cover properties and avalanche dynamics	12
17:00–17:15	Callegari, Mattia	EURAC research- Institute for Applied Remote Sensing	250 meters resolution daily snow cover maps and a novel cloud filter based on topographic snow cover patterns learning with Support Vector Machine	13
17:15–17:30	Sukhodolov, Timofei	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	Sensitivity of the photolysis rate to the uncertainties in spectral solar irradiance variability	14

Wednesday, September 10, 2014

17:30–18:30 Podium «Expectations and needs of young academics»

Richards, R. Geoff	AO Research Institute	Chair
Bühler, Yves	WSL Institute for Snow and Avalanche Research SLF	Project Leader
Cessateur, Gaël	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	Postdoctoral researcher
Follonier, Stéphane	CSEM Landquart	Director
Gardner, Oliver	AO Research Institute	Doctoral candidate
Huitema, Carly	Swiss Institute of Allergy and Asthma Research	Postdoctoral researcher
Schweiger, Anna	Parc Naziunal Svizzer	Doctoral candidate

18:50–19:50 Keynote Lecture Allergy Education Week

French, Lars	Universitätsspital Zürich	Heilmittel als Krankheitsauslöser: Arzneimittel-allergien
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20:30 Dinner Waldhotel Davos

Thursday, September 11, 2014

08:30–10:30 Oral Presentations: Natural and Technical Sciences

	Follonier, Stéphane	CSEM Landquart	Chair
	Stuflesser, Werner	European Academie of Bozen/ Bolzano	Chair
08:30–09:00	Bebi, Peter	WSL Institute for Snow and Avalanche Research SLF	Keynote: Future provision of ecosystem services in mountain regions – how can science help?
09:00–09:15	Cessateur, Gaël	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	Rising of the 24th solar cycle 15
09:15–09:30	Adams, Wilnelia	Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center	A new model for solar irradiance of the past and forecasts into the future 16
09:30–09:45	Müller, David	CSEM Landquart	Analysis of nanoparticle-containing sunscreens with a miniaturized Asymmetrical Flow Field-Flow Fractionation cartridge 17
09:45–10:00	Procter, Emily	EURAC research – Institute of Mountain Emergency Medicine	Recreational activity in avalanche terrain: Influence of group size on avalanche risk 18
	Zweifel, Benjamin	WSL Institute for Snow and Avalanche Research SLF	
10:00–10:15	Simioni, Stephan	WSL Institute for Snow and Avalanche Research SLF	Field experiments on weak layer failure and crack propagation due to avalanche control by explosives 19
10:15–10:30	Ganthalder, Andrea	alpS	Infection of Norway spruce by the pathogen <i>Chrysomyxa rhododendri</i> : Analysis of infection dynamics and establishment of resistant trees 20

10:30–11:30 Poster Presentations (P15–25): Medical Sciences

	Crameri, Reto	Swiss Institute of Allergy and Asthma Research	Chair
	Reinhart, Walter	Academia Raetica	Chair
	Eberli, Ursula	AO Research Institute	Non-invasive biomechanical monitoring of bone healing in a dynamized bone defect in sheep P15
	Gardner, Oliver	AO Research Institute	Improving the quality of surgical cartilage repair P16
	Hasselmann, Viviane	Kliniken Valens	Are serious games promoting mobility an attractive alternative to conventional self-training for elderly people? P17

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Helfen, Tobias	AO Research Institute	Kortikale Dicke und Porosität am proximalen Humerus korrelieren mit dem osteoporotischen Knochensubstanzverlust: Eine Analyse der mikrostrukturellen Umbauprozesse	P18
Huitema, Carly	Swiss Institute of Allergy and Asthma Research	Quantitative measurements of antigen-specific immunoglobulins using an evanescent biosensor	P19
Johannson, Bettina	Kantonsspital Graubünden	Medial bony support as an indicator for the selection of the osteosynthesis procedure in complex bicondylar proximal tibia fractures	P20
Olzhausen, Judith	Swiss Institute of Allergy and Asthma Research	Measurements of allergen specific antibodies during allergen specific immunotherapy using the evanescent field method: A comparison	P21
Peiffer, Simon	Kantonsspital Graubünden	Bilocal recurrence of a neuroendocrine carcinoma of the small intestine	P22
Sprecher, Christoph	AO Research Institute	Der zementfreie Oberflächenersatz der Schulter induziert ein knöchernes Stress-Shielding: Eine humane Explantate- und Finite-Elemente-Analyse	P23
Stanciuc, Ana-Maria	AO Research Institute	Characteristics of human primary osteoblasts from osteoarthritic femoral heads	P24
Wawrzyniak, Marcin	Swiss Institute of Allergy and Asthma Research	Isolation and characterization of IL-22 producing T cells	P25

11:30–13:00 Lunch and Poster Viewing with CK-CARE Allergy Education Week

13:00–14:00 Oral Presentations: Humanities

Hitz, Florian	Institut für Kulturforschung Graubünden	Chair	
Tomaschett, Carli	Institut dal Dicziunari Rumantsch Grischun	Chair	
13:00–13:15	Mitterhofer, Johanna	EURAC research – Institute for Minority Rights	«Old» and «new» minorities: perspectives on migration and identity in South Tyrol 21
13:15–13:30	Ellemunter, Lisa	EURAC research – Institute for Minority Rights	ID-Coop: Identity and cooperative enterprise in areas inhabited by linguistic minorities 22
13:30–13:45	Lutz, Ursin	Institut dal Dicziunari Rumantsch Grischun	Balthasar Gioseph de Vincenz (1789–1858) und sein Meum Scret 23
13:45–14:00	Bundi, Simon	Institut für Kulturforschung Graubünden	Wege des Gemeindedualismus. Eine Geschichte der Bündner Bürgergemeinden 1874–1974 24

14:00–15:00 Oral Presentations: Natural Sciences and Interdisciplinary Topics

Pielmeier, Christine	WSL Institute for Snow and Avalanche Research SLF	Chair	
Schneider, Erich	Academia Raetica	Chair	
14:00–14:15	Roth, Andrea	Global Risk Forum GRF Davos	How safe is safe enough? A methodology for defining protection targets for critical infrastructures and services 25
14:15–14:30	Sättele, Martina	WSL Institute for Snow and Avalanche Research SLF	Reliability analyses provide guidance to cost-efficient early warning systems for natural hazards 26
14:30–14:45	Rohrbach, Benjamin	University of Zurich	Participatory mapping: A tool for participatory policy development in protected areas 27
14:45–15:00	Klotz, Greta Trettel, Martina	EURAC research – Institute for Studies on Federalism and Regionalism	Der Alpenraum als Labor der grenzüberschreitenden Zusammenarbeit: Der EVTZ «Europaregion Tirol-Südtirol-Trentino» und die makroregionale Strategie für die Alpen 28

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15:00–16:00 Oral Presentations: Medical Sciences

	Richards, R. Geoff Rüedi, Thomas	AO Research Institute Academia Raetica	Chair Chair
15:00–15:15	Camartin, Cristian	Kantonsspital Graubünden	Patienten mit einem Bronchuskarzinom auf einer Palliativstation – Eine prospektive Studie über die Symptome und deren Behandlung 29
15:15–15:30	Schraffl, Daniel	Kantonsspital Graubünden	Results and postoperative quality of life in patients greater than 80 years old after colorectal surgery 30
15:30–15:45	Prati, Moira	Swiss Institute of Allergy and Asthma Research	Preventive/therapeutic vaccines in a murine model of allergy 31
15:45–16:00	Vöggtli, Daniela	AO Research Institute	Parametric analysis of proximal femur morphology on fracture behavior in sideways fall situations 32

16:00–16:30 Coffee Break

16:30–17:45 Podium «Forschung, Lehre und Innovation in Graubünden»

	Waser, Norbert		Moderation
	Flury, Johannes	Pädagogische Hochschule Graubünden	Ehem. Rektor
	Märchy, Hans Peter	Amt für Höhere Bildung, Kanton Graubünden	Leiter
	Minsch, Rudolf	Innovationsstiftung Graubünden	Stiftungsrat
	Müller, Urs	GRITEC AG	CEO
	Schweizer, Jürg	WSL-Institut für Schnee- und Lawinenforschung SLF	Leiter

17:45–18:30 Award Ceremony Graduate School Graubünden & Young Scientists in Contest

18:30 Apéro

ORAL PRESENTATIONS

1

Epigenetic mechanisms for weaker expression of tight junctions in bronchial epithelial cells from asthmatic individuals

Wawrzyniak Paulina^{1,2}, Akdis Cezmi A.^{1,2}, Akdis Mübeccel^{1,2}, Ban-delja Kreso⁴, Jakiela Bogdan³, Kast Jeannette I.^{1,2}, Rückert Beate^{1,2}, Sanak Marek³, Wanke Kerstin^{1,2}, Wawrzyniak Marcin^{1,2}

¹ Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

² Christine Kühne-Center for Allergy Research and Education, Davos, Switzerland

³ Jagiellonian University, Krakow, Poland

⁴ Institute of Immunology Inc., Zagreb, Croatia

Background: Tight junction (TJ) proteins, located at the apical part of the cells, form the epithelial barrier, which prevents the tissue penetration of environmental agents such as allergens, pollutants, and bacterial toxins. Defects in bronchial epithelial TJs may lead to loss of barrier function and play a role in initiation and chronicity of asthma and may be controlled by epigenetic mechanisms.

Aim: The regulation of bronchial epithelial TJs by Th2 cells and their cytokines on bronchial epithelial cells from healthy and asthmatic individuals was investigated.

Methods: Primary human epithelial cells from healthy and asthmatic donors were cultured in air-liquid interface (ALI) and stimulated with Th2 cells, cytokines, and a histone-deacetylase inhibitor. Transepithelial resistance, paracellular flux, TJ mRNA, and protein expression were determined.

Results: Asthmatic bronchial epithelial cells showed an inherited low TJ integrity compared to control epithelial cells, which was consistent even after several passages of the cells. Th2 cells and their cytokines IL-4 and IL-13 decreased transepithelial resistance and increased paracellular flux in control, but not in asthmatic bronchial epithelial cells. Bronchial epithelial cell stratifications suggesting opening of TJs were observed in immunofluorescence staining of the adaptor protein ZO-1 and occludin. We observed also weaker expression of occludin in asthmatic epithelium compared to healthy controls. To investigate the epigenetic mechanisms responsible for the differences between healthy and asthmatic bronchial epithelial cells, we incubated the cells with the histone deacetylase inhibitor JNJ-26481585. We observed a recovery of barrier integrity with increased transepithelial resistance and upregulation of the tight junction mRNAs, as well as increased expression of occludin in immunofluorescence staining.

Conclusion: Our data demonstrate that Th2 cells and their cytokines downregulate the integrity of bronchial epithelial cells. Inhibition of endogenous histone deacetylase activity corrected the defective barrier by upregulation of the expression of tight junction molecules.

2

Generation and characterization of human allergen-specific B cell clones

van de Veen Willem¹, Akdis Cezmi¹, Akdis Mübeccel¹, de Jong Marlein², Kwakkenbos Mark³, Ochsner Urs¹, Spits Hergen², Stanic Barbara¹, van Splunter Marloes¹, Wirz Oliver¹

¹ Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

² Academic Medical Center, Tytgat Institute for Liver and Intestinal Research, Amsterdam, Netherlands

³ AIMM Therapeutics, Amsterdam, Netherlands

High-dose exposure can induce immunological tolerance to certain allergens. During allergen-specific immunotherapy (SIT) allergen-specific IgG4 is frequently increased. Beside changes in circulating allergen-specific immunoglobulins, little is known about the regulation of B cell responses during SIT. This study aims to investigate the effect of high-dose antigen exposure on the function and phenotype of allergen-specific memory B cells. Characterization of human antigen-specific B cells has been hampered by the fact that long-term culture of B cells is chal-

lenging. In this study we generated long-living allergen-specific memory B cells.

Peripheral memory B cells from non-allergic individuals, bee venom-allergic patients and beekeepers were immortalized by transduction with *BCL-6* and *Bcl-xl*, leading to formation of proliferating, BCR-positive, immunoglobulin-secreting cells. B cells were isolated using labelled phospholipase A2 (PLA). We measured the frequency of PLA-specific B cells and generated PLA-specific B cell clones.

Non-allergic individuals did not have detectable PLA-specific memory B cells, whereas frequencies of PLA-specific cells in beekeepers and BV-allergic patients reached up to 0.4%. Beekeeper-derived PLA-specific B cells were mainly IgG4-switched. The frequency of IgG4⁺ cells within PLA-specific B cells from BV-allergic patients was > 10-fold increased after bee venom-specific immunotherapy (SIT). Furthermore, IgG4⁺ B cell clones showed increased expression of HLA-DR and CD86 when compared to IgG1⁺ clones. Secretion of TNF-alpha, RANTES, IL-6, IP-10 and CCL4 was significantly reduced in IgG4-switched clones.

Here we show the isolation and culture of human *in vivo* switched allergen-specific memory B cells. This approach will provide insight into the mechanisms at the B cell level that drive immune tolerance towards allergens. Allergen-specific B cells showed an increased frequency of IgG4-switched cells after SIT. We found that CD86 and HLA-DR were upregulated in IgG4⁺ compared to IgG1⁺ B cells, indicating that IgG4⁺ cells may be efficient antigen-presenting cells. Furthermore, IgG4⁺ B cell clones show reduced production of pro-inflammatory cytokines and chemokines.

3

Acetylation of SERCA2a: A new potential strategy to modulate calcium dynamics

Florio Maria Cristina¹, Corti Corrado¹, Domingues Francisco¹, Piubelli Chiara¹, Pompilio Giulio², Pramstaller Peter P.¹, Rossini Alessandra¹, Volpato Claudia¹, Weichenberger Christian¹

¹ Center for Biomedicine, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italy, affiliated Institute of the University Lübeck, Germany

² Laboratory of Vascular Biology and Regenerative Medicine, Centro Cardiologico Monzino, IRCCS, Milano, Italy

Acetylation at specific lysine (K) residues is one of the most biologically relevant modifications, involved in the regulation of various processes, including cell migration and nucleocytoplasmic shuttling of proteins (Sadoul K et al, J Biomed Biotechnol, 2011). The enzymes responsible for protein acetylation and deacetylation are known as histone acetyltransferases (HATs) and histone deacetylases (HDACs) but may act both on histone and non-histone proteins. Within the context of cardiac function increased acetylation of sarcomeric proteins by HDAC inhibition has been demonstrated to enhance the myofilament calcium sensitivity and, consequently, their contractile activity (Gupta MP et al, J Biol Chem, 2008). Preliminary experiments indicate that HDAC inhibition promoted by SAHA (Suberoylanilidehydroxamic acid, a general HDAC inhibitor) treatment may result in an increased efficiency of calcium (Ca²⁺) re-uptake in isolated adult zebrafish ventricular myocytes. Ca²⁺ ATPase SERCA2a plays a pivotal role in the recovery phase of calcium transient, regulating both cytosolic Ca²⁺ concentration and sarcoplasmic reticulum (SR) calcium load. Therefore, we investigated whether SERCA2a direct acetylation may be involved in the SAHA-dependent observed effect by co-immunoprecipitation experiments of SERCA2a and total acetyl-lysines on HL-1 cell lysates, resulting in a significant increase in the acetylation of SERCA2a after HDAC inhibition treatment. This result sustains our hypothesis that the protein can be directly acetylated. Identification of putative acetylated lysines, performed by bioinformatic analysis, indicated that SERCA2a possesses a consistent number of lysines that can be acetylated and are highly conserved among different species. To confirm that direct acetylation can modulate SERCA2a activity further experiments will be performed, such as mass spectrometry analysis, measurements of SERCA2a activity carried on isolated microsomes and records of calcium transients in isolated rat cardiomyocytes. The fulfillment of the proposed project will open new perspectives on the search for innovative pharmacological tools

to treat diseases associated to altered calcium handling, such as heart failure and diabetic cardiomyopathy.

4

Effects of lipids and cholesterol on the chondrogenesis of human mesenchymal stem cells

Makwana Priyanka, Alini Mauro, Gardner Oliver, Stoddart Martin
AO Research Institute, Davos, Switzerland

Adult articular cartilage does not possess any blood vessels or nerves, thereby limiting the repair capabilities to regrow the tissue. Thus even minor injury or trauma could lead to progressive damage and osteoarthritic degeneration, leading to significant pain and disability. Degenerative joint diseases are widespread in countries with high life expectancy. While there are numerous surgical techniques available to treat defect such as arthroscopy and joint replacements, the treatments are not able to alleviate pain completely. A cell therapy known as autologous chondrocyte transplantation was developed more than two decades ago to regenerate tissue. In this case, cells that make cartilage (chondrocytes) are obtained from biopsies of normal patient tissue, and are expanded to increase cell number followed by injection into the defect. However, the regenerated tissue possesses poor functionality and quality. With the development of regenerative medicine, adult stem cells have unleashed potential for the regeneration of cartilage, providing an alternative approach to treat cartilage defects. These cells have an ability to differentiate into various cell types. These differentiated cells can produce matrix similar to articular cartilage. In this study, we cultured human mesenchymal stem cells into pellets to generate tissue having similar properties to the articular cartilage. These cells were cultured in presence of lipids and cholesterol along with four different kinds of cell media such as DMEM, F-12, Mega Cell and ExCell. From the four different media, DMEM out performs in context of maintaining chondrogenesis. Furthermore, lipids have been seen to enhance chondrogenesis in pellet culture while cholesterol has an inhibitory effect on the chondrogenesis. This study has revealed the different effects of nutrition on the ability of human mesenchymal stem cells to regenerate tissue.

5

Biomimetic nucleus pulposus replacement for the treatment of degenerative disc disease

Lang Gernot¹, Alini Mauro¹, Chen Xu¹, Grad Sibylle¹, Li Zhen¹, Sacks Hagit², Yayon Avner³

¹ AO Research Institute, Davos, Switzerland

² Nicast Ltd., Lod, Israel

³ Procure Ltd., Nes Ziona, Israel

Introduction: Degeneration of the intervertebral disc (IVD), containing the gelatinous nucleus pulposus (NP), surrounded by the fibrocartilaginous annulus fibrosus (AF), is a major cause for low back pain, which is the most frequent reason for inability to work in Western civilizations. NP replacement offers a minimally invasive alternative to traditional therapies for degenerative disc disease. Recently a novel polyurethane scaffold with swelling capability and a fibrinogen-hyaluronic acid hydrogel were developed to restore native disc mechanical and biological properties, by mimicking the NP extracellular matrix. The aim of this study is to evaluate the scaffold and the hydrogel in an organ culture system with dynamic load.

Materials and Methods: Intervertebral discs from bovine tails were nucleotomized and refilled with either (1) scaffold, (2) scaffold surrounded by the hydrogel or (3) hydrogel. Empty discs (E) served as negative controls. To assess the mechanical compatibility of the different implants, dynamic compressive stiffness modulus and disc height were measured for each disc at different time points: Intact, after nucleotomy, after refilling with biomaterial and free swelling recovery overnight, after 3 h dynamic load at 0–0.1 MPa, 0.1 Hz within a bioreactor system and after free swelling recovery overnight.

Results: After nucleotomy, stiffness dropped to 30% compared with intact discs. After refilling with the scaffold, stiffness was

restored to 73%. After load and recovery the stiffness of the scaffold-refilled discs increased to 82%. While the hydrogel delayed the restoring effect, stiffness also increased to 69% after load and recovery. Disc height of all three implant groups was maintained after loading and recovery.

Conclusion: The swelling scaffold is able to restore the mechanical property and the disc height, which is essential to prevent further disc degeneration. Furthermore, addition of the fibrin-hyaluronan hydrogel may result in improved biological repair.

Acknowledgment: Funded by the European Commission under the FP7-NMP Project NPMimetic.

6

Assessing the role of implant stability on the development of staphylococcal osteomyelitis in a murine fracture model

Sabaté Brescó Marina^{1,2}, Kluge Katharina¹, Moriarty Fintan¹, O'Mahony Liam², Richards, R. Geoff¹, Ziegler Mario²

¹ AO Research Institute, Davos, Switzerland

² Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

Introduction: Implant instability is considered a risk factor for delayed healing of fractures and infection; however, little experimental data is available confirming this belief, or describing the underlying mechanisms. In this study, a murine model based upon the MouseFix™ system (RISystem AG, Davos)^{1,2} was used to investigate immune response in bone when fractures are fixed with rigid or non-rigid (i.e. flexible) constructs. Implant associated osteomyelitis was developed in some groups using a clinical isolate of *Staphylococcus epidermidis*, one of the leading etiologic agents of orthopedic infections³. The development of infection and immune responses associated with either rigid or flexible implants was assessed.

Methods: Rigid and flexible MouseFix™ titanium plates, with or without *Staphylococcus epidermidis* (10⁴ CFU) contamination, were used with a femoral osteotomy in C57Bl/6 mice (female, 20–26 week old). Mice were sacrificed at 7, 14, and 30 days after surgery (n=6–9 per group). Live bacteria from the implant, bone, and soft-tissue were quantified. Bone and spleen cells were kept for mRNA analysis and stimulated to collect supernatants for cytokine and chemokine quantification. Lymph node and bone cells were characterized by flow cytometry.

Results: At each time-point over 30 days, unstable fractures had a higher infection rate compared to stable fractures. Monocytic lineage cells (F4/80+) increased in percentage over time in all four conditions, probably due to macrophage recruitment, but slightly more in animals with flexible implants suggesting a role of these cells. In lymph node, IL-17+ cells were increased at early time-points in infected animals, especially in those where bacteria were not detected. Levels of IL-10+ cells were similar between all groups at 7 days, increasing in not-infected animals later. When studying IL-17+/IL-10+ ratio in CD3+CD4+ cells, animals with flexible devices seemed to be skewed to a more anti-inflammatory response, which could explain differences observed.

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7

Die Kirchenanlage Sogn Murezi in Tomils (GR) – kirchliches und herrschaftliches Zentrum im frühmittelalterlichen Churrätien

Jecklin-Tischhauser Ursina

Kunsthistorisches Institut, Lehrstuhl für Kunstgeschichte des Mittelalters, Archäologie der frühchristlichen, hoch- und spätmittelalterlichen Zeit, Universität Zürich, Schweiz

Die Kirchenanlage Sogn Murezi in Tomils (Domleschg/ GR) gehört neben dem Kloster St. Johann in Müstair (GR) und dem Kathedral-komplex von Genf zu den archäologisch am besten untersuchten

Kirchenanlagen der Schweiz. Angesichts der Grösse der Anlage und der überregionalen Bedeutung der Baureste wurde Sogn Murezi vom Bund als Kulturgut von nationaler Bedeutung (Kategorie A) eingestuft und unter eidgenössischen Schutz gestellt.

Zum Baukomplex, der sein Aussehen vom 7. bis ins 10. Jh. erheblich verändert hat, zählte eine Kirche mit mehreren zugehörigen Wohn- und Wirtschaftsbauten. Aber bereits vor der eigentlichen Kirchenanlage, nämlich ab dem 5. Jahrhundert existierten an derselben Stelle Gebäude in Holz oder Stein. In der ersten Hälfte des 10. Jh. wurden die An- und Nebenbauten der Kirche abgerissen und die Kirche fungierte bis zu ihrer Auflassung im 15. Jh. als freistehende Pfarrkirche mit Friedhof.

Der hervorragende Erhaltungszustand der Gebäude und deren Einrichtung bietet die seltene Gelegenheit, architekturgeschichtliche, bautechnische, funktionale und liturgische Aspekte exemplarisch zu untersuchen. Auch das ausgegrabene Fundmaterial stellt für die Frühmittelalter-Forschung einen bedeutenden Quellenzuwachs dar.

Schriftliche Quellen zur Kirchenanlage existieren keine. Hinsichtlich der Funktion der Anlage lassen die Funde auf eine klerikale Gemeinschaft schliessen, die die Anlage betreute und an verkehrstechnisch günstiger Lage entlang der Hauptroute über die Alpenpässe seelsorgerische, aber auch profane Verwaltungsaufgaben wahrgenommen hat. Die bauliche Qualität und die reiche Ausstattung der Räume, die Speisreste, deren Auswertung einen geradezu luxuriösen Speisezettel ergab sowie der Umstand, dass in und um die Anlage nie bestattet wurde, deuten auf eine adelige Stiftung hin.

Sogn Murezi war aufgrund seiner Grösse und Ausstattung ohne Frage ein wichtiges herrschaftliches und kirchliches Zentrum der Region. Vor dem Hintergrund der territorialpolitischen Ereignisse der damaligen Zeit gilt es, die Funktion und kulturhistorische Bedeutung der Anlage sowie die im Laufe der Jahrhunderte wandelnden Rechts- und Besitzverhältnisse zu ergründen. Die Disziplinen übergreifende Auseinandersetzung mit der Kirchenanlage lässt auf neue Erkenntnisse zur Grundherrschaft, zur Kirchen-, Verwaltungs- und Pfarreiorganisation Churrätens und des nordöstlichen Alpenraums hoffen.

8

Scientific analysis of human remains: From the Egyptian mummy of the Natural History Museum of Venice-Italy, to the medieval skeletons of South Tyrol-Italy

Paladin Alice, Zink Albert

Institute for Mummies and the Iceman, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italy

Human remains are concrete and direct evidence of life in the past. In fact, the scientific study of mummies and skeletons allows us to explore the history of ancient populations, to understand where and how people lived; the way they adapted to different environments; their diets; their health conditions and their daily activities. Different methods ranging from physical anthropology, paleopathology, molecular biology (ancient DNA) and geochemistry (stable isotopes) permit the analysis of the human remains from different perspectives. Starting from a single mummy through to a larger series of skeletons, we will demonstrate how the analysis of the remains has developed and what are the methodologies, questions and problems.

The Natural History Museum of Venice, Italy, houses an Egyptian mummy (MSNVE-7696) found in the Crocodile Grotto, nearby Manfalut. Initially, we performed an in-depth research on the history and the finding place of that mummy. In 2010, computer tomography scanning permitted anthropological, paleopathological and conservation studies to be carried out. The mummy was a 50–60 year old woman: The investigation revealed pathological signs, a high-level of post mortem alterations, an inaccurate mummification and more details about the methods of the conservation in the 19th century.

The analysis of human remains is an important support for the archaeological research. For example, based on the archaeological records of the medieval South Tyrol, Italy, it is still unclear in what way and to what extent the Germanic groups interacted with the local population and whether the noted cultural change was due to admixture or rather replacement events. Therefore, we start-

ed a multidisciplinary PhD project for a detailed anthropological, paleopathological and stable isotope analysis of more than 200 skeletons from different Tyrolean sites. First results of this study will be introduced, providing insights into the health conditions and occupational markers of the medieval skeletons.

9

^kAltes Eis – Gletscherarchäologie in Graubünden

Naef Leandra

Institut für Kulturforschung Graubünden, Chur, Schweiz

Das durch die anhaltende Klimaerwärmung abschmelzende «ewige Eis» der Alpen gibt nicht nur bisher unzugängliches Neuland, sondern auch einzigartige Relikte aus der Vergangenheit frei. Das immense kulturgeschichtliche Potential dieses Eisarchivs ist erstmals durch den Fund des 5300 Jahre alten Eismannes «Ötzi» 1991 deutlich geworden. Seither belegen aussergewöhnliche (prä)historische Funde aus dem gesamten Alpenraum, dass es sich hierbei keineswegs um einen Einzelfall handelte.

Die relative Berechenbarkeit der bisher bekannten Deponierungsmuster erlaubt es sogar, potentielle Eisfundstellen mit Hilfe komplexer Modelle zu berechnen. Dieses im geisteswissenschaftlichen Kontext zunächst ungewöhnlich anmutende, jedoch effiziente und zielgerichtete Konzept bildet die Ausgangslage für eine systematische Gletscherarchäologie in Graubünden.

Ein entsprechendes Modell wurde – analog zu den bisher bekannten Eisfunden – ausgehend von der Kartierung sämtlicher hochalpiner Pässe erstellt. Auf Grund ihrer Topographie kanalisieren diese natürlichen Lücken und Jöcher seit Jahrtausenden unterschiedliche menschliche Aktivitäten im Gebirge (Handel, Jagd, Alpwirtschaft, Rohstoffgewinnung, Alpinismus etc.) und weisen als natürliche Mobilitätskorridore folglich ein deutlich erhöhtes (gletscher-)archäologisches Potenzial auf. Diese rund 600 hochalpinen Übergänge Graubündens wurden mittels eines GIS in einem mehrstufigen Bewertungsverfahren anhand ihrer verkehrsgeographischen Lage, relevanter topographischer Parameter, mittels Luftbildern sowie historischer und archäologischer Daten nach ihrem spezifischen Funderwartungspotential bewertet, selektiert und in einer abschliessenden Vorhersagekartierung zusammengefasst.

Vorrangiges Ziel des daraus hervorgegangenen Projektes «^kAltes Eis» ist die praktische Umsetzung der theoretischen Grundlagenarbeit auf den drei Wirkungsebenen Forschung – Praxis – Öffentlichkeit. Bis Ende 2015 werden die ermittelten Fundverdachtsflächen gezielt begangen, dokumentiert und überwacht, um mögliche archäologische Objekte aus dem Eis zu sichern. Die Geländearbeiten sind explizit transdisziplinär ausgerichtet und sollen dieses Programm so zu einer Modellstudie für den gesamten Alpenraum machen.

Neben der zeitlich und räumlich begrenzten wissenschaftlichen Geländearbeit stellt ein Awareness-Programm den zweiten wesentlichen Bestandteil des Massnahmenkatalogs zur Sicherung klimatisch bedrohter Eisfunde dar. Das Zielpublikum (v.a. Wanderer und Bergsteiger) soll dabei im unmittelbaren alpinen Umfeld über die Bedrohung und das wissenschaftliche Potential von Eisfunden aufmerksam gemacht werden. Dies soll dazu beitragen, dass auch vermeintlich unspektakuläre Beobachtungen und Funde dokumentiert und an die richtige Stelle weitergeleitet werden.

10

Demographic and cultural factors in shaping the genetic variation of alpine ethno-linguistic groups

Coia Valentina¹, Anagnostou Paolo², Battaglia Cinzia², Capocasa Marco³, Cipollini Giovanna¹, Destro-Bisol Giovanni^{2,4}, Maixner Frank¹, Zink Albert¹

¹ Institute for Mummies and the Iceman, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italy

² Dipartimento Biologia Ambientale, Università La Sapienza, Rome, Italy

³ Dipartimento Biologia e Biotecnologie «Charles Darwin», Università La Sapienza, Rome, Italy

⁴ Istituto Italiano di Antropologia, Rome, Italy

The Alps are inhabited by a mosaic of ethno-linguistic minorities (e.g. Franco-Provençals, Occitans, French, Slovenes, Germans and Ladins), whose geographical isolation has helped maintain most of their cultural traditions. A remarkable population diversity may be found even in subdivisions of the alpine arch, such as the Eastern Italian Alps, a relatively small area where groups of different language and social structure (Italian, Ladin and German) are settled. For this reason, the Alps offer a unique opportunity to investigate the role of cultural factors in shaping the genetic structure of European populations.

In this study we present an analysis of high resolution Y Chromosome data (17 STRs and 50 SNPs) in 15 alpine populations (a total of 610 individuals) belonging to the three main ethno-linguistic groups of the Eastern Italian Alps. We investigated the relationships between genetic and linguistic diversity and extended the analysis to mtDNA data to explore signatures of a gender biased gene flow among groups.

We observed a low and insignificant level of variation among linguistic groups ($p > 0.05$), while no pattern of linguistic structuring of genetic variation was detected by the analysis of the genetic distances. These results suggest that language is a poor predictor of genetic diversity, consistent with previous mtDNA data for the same populations. On the other hand, a high level of genetic variation was found among German and Ladin-speaking groups (26% and 7%, respectively). This result may be accounted for by the effect of genetic drift, in accordance with historical and demographic data. Finally, we found a strikingly different genetic pattern of Y-chromosomal and mtDNA intra-group diversity between Tyroleans and other groups under study probably related to an increased male mobility associated with the practice of the «Geschlossener Hof» in south Tyrolean communities.

11

Spatial movement patterns and high-resolution remote sensing data explain resource selection of three sympatric ungulate species

Schweiger Anna K.^{1,2,3}, Anderwald Pia¹, Haller Rudolf¹, Kneubühler Mathias², Risch Anita C.³, Schaepman Michael E.², Schütz Martin³

¹ Swiss National Park, Zernez, Switzerland

² Remote Sensing Laboratories, Department of Geography, University of Zurich, Zurich, Switzerland

³ Swiss Federal Institute for Forest, Snow and Landscape Research WSL, Birmensdorf, Switzerland

The potential for interspecific competition between large ungulates remains an important topic in the conservation of their communities. Interspecific competition often results from the use of the same depletable resources, such as forage. Founded in 1914, the Swiss National Park (SNP) is the oldest national park in the Alps and Central Europe. Due to its strong protection status remarkably high densities of ibex, chamois, and red deer can be found in the SNP and, in particular, in the valley of Trupchun. Since the year 2000 the SNP's GPS (Global Positioning System) radio collaring project has collected GPS data from individuals of all three species. These data reveal that the habitats of ibex and chamois are largely overlapping, while red deer seem to choose different areas for foraging. However, the reasons for their spatial distribution remained unknown, since spatially continuous high-resolution environmental data were missing. However, joining GPS data with high-resolution maps of resource availability is a key for the differential analyses of the requirements of single ungulate species and for detecting potential overlaps between species. We used data from the airborne imaging spectrometer APEX collected during four growing seasons (2010–2013) to estimate and map resource availability (biomass, nitrogen, fibre content of the vegetation) at very high spatial resolution (2 x 2 m pixel size). These maps served as baseline data to analyse the ungulates' movement patterns. More specifically, we applied step-selection functions and conditional logistic regressions to describe the foraging behaviour of the three species separately. We then compared the species spatial behaviour and explored differences and similarities in their resource use. Our results show how the partitioning of resources in space and time shape interactions in this animal guild – valuable information for the species' future conservation.

12

Linking snow cover properties and avalanche dynamics

Steinkogler Walter^{1,2}, Lehning Michael^{1,2}, Sovilla Betty¹

¹ WSL-Institute for Snow and Avalanche Research SLF, Davos, Switzerland

² CRYOS, School of Architecture, Civil and Environmental Engineering, EPFL, Lausanne, Switzerland

Avalanches exhibit many different flow regimes from powder clouds to slush flows with fundamentally different flow dynamical characteristics, such as velocities and run-out distances. To explain these varying flow dynamics the snow cover properties must be taken into account. Recent investigations showed that the temperature of the flowing snow is one of the most important factors controlling the avalanche typology and thus the flow dynamics. Our investigations allowed for the first time to quantify the relative contribution of the temperature in the released and entrained snow versus the temperature increase from frictional processes.

Additionally, it was found in laboratory experiments that below a temperate threshold of -1°C a significant densification could be observed, yet the moving particles remained individual and cohesionless at the crystal scale. Such cold and dry snow is typically found in dry-dense flowing and powder avalanches. As soon as the snow was warmer than -1°C , distinct granules of varying sizes and properties formed and resulted in much more cohesive and larger particles, as found in moist and wet avalanches. These variations and transitions in granule structures allow to describe different flow dynamics and to establish a link to snow temperature. The results of this study are of significant interest for engineering problems, enhancements of avalanche dynamics models, and forecasting. For example, snow safety personnel should be aware of snow cover property variations, e.g. altitude of 0°C line, since unexpected and atypical avalanche flow behavior, such as variations in expected run-out distance and flow direction, can occur.

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250 meters resolution daily snow cover maps and a novel cloud filter based on topographic snow cover patterns learning with Support Vector Machine

Callegari Mattia, Costa Armin, Cuozzo Giovanni, De Gregorio Ludovica, Monsorno Roberto, Notarnicola Claudia, Padovano Antonio, Ventura Bartolomeo, Zebisch Marc
Institute for Applied Remote Sensing, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italy

Most of hydrological events in Alpine regions are mainly regulated by snow, especially during the melting season. Daily snow cover maps are available thanks to the Moderate Resolution Imaging Spectroradiometer (MODIS) sensor, mounted over Terra and Aqua satellites. However, two main limitations are related to this product. Its coarse resolution, equal to 500m, is critical especially in Alpine areas where the snow cover spatial variability is very high due to the irregular topography. The second issue is related to clouds, which do not allow the MODIS sensor to acquire any land surface information. A novel product for mitigating these two issues, which may drastically affect the accuracy of the snow cover extent estimation, is here proposed. Daily 250m resolution snow maps are obtained through the algorithm described in (1) providing an improved snow cover mapping approach with respect to the standard 500m MODIS product. The algorithm was developed specifically for mountain areas. The snow cover detection is based on MOD09GQ-MYD09GQ 250m NDVI (Normalized Difference Vegetation Index) using atmospherically corrected surface reflectances. The cloud detection is done with MOD09GA-MYD09GA products (500m resolution) and MOD021KM-MYD021KM (1km resolution). MOD03-MYD03 are used for correct geolocation. The accuracy of this new algorithm was found to vary between 90% and 94% when compared with LANDSAT snow maps and ground data respectively. Details on the validation results are described in (2). The clouds problem is mitigated applying standard time filters, which exploit the time correlation of snow cover, and implementing a novel spatial filter based on Support Vector Machine (SVM).

The proposed approach exploits topographic information such as altitude and aspect. By learning topographic snow cover patterns under clear sky scenarios it is able to estimate the presence of snow under clouds by looking at the surrounding no cloudy pixels. References: (1) Notarnicola, C.; Duguay, M.; Moelg, N.; Schellenberger, T.; Tetzlaff, A., Monsorno, R.; Costa, A., Steurer, C.; Zebisch, M. Snow cover maps from MODIS Images At 250m resolution, Part 1: Algorithm Description, Remote Sensing, 2013, 5, 110-126. (2) Notarnicola, C.; Duguay, M.; Moelg, N.; Schellenberger, T.; Tetzlaff, A., Monsorno, R.; Costa, A., Steurer, C.; Zebisch, M. Snow cover maps from MODIS images At 250m resolution, Part 2: Validation, Remote Sensing, 2013, 5, 1568-158.

14

Sensitivity of the photolysis rate to the uncertainties in spectral solar irradiance variability

Sukhodolov Timofei¹, Bais Alkiviadis², Bossay Sébastien³, Chipperfield Martyn⁴, Fomin Boris⁵, Peter Thomas⁶, Rozanov Eugene^{1,6}, Sander Rolf⁷, Schmutz Werner¹, Shapiro Alexander¹, Smyshlyayev Sergey⁸, Telford Paul⁹, Tourpali Kleareti⁶

¹ Physikalisches-Meteorologisches Observatorium Davos/ World Radiation Center, Davos, Switzerland

² Laboratory of Atmospheric Physics, Aristotle University of Thessaloniki, Thessaloniki, Greece

³ Laboratoire Atmosphères, Milieux, Observations Spatiales, Université de Versailles Saint-Quentin-en-Yvelines Paris, France

⁴ Institute for Climate and Atmospheric Science, School of Earth and Environment, University of Leeds, United Kingdom

⁵ Central Aerological Observatory (CAO), Moscow, Russia

⁶ Institute for Atmospheric and Climate Science, ETH Zurich, Zurich, Switzerland

⁷ Max-Planck-Institut für Chemie, Mainz, Germany

⁸ Russian State Hydrometeorological University, Saint Petersburg, Russia

⁹ National Centre for Atmospheric Science, University of Cambridge, Cambridge, United Kingdom

The state of the stratospheric ozone layer and temperature structure are mostly maintained by the photolytical processes. Therefore, the uncertainties in the magnitude and spectral composition of the spectral solar irradiance (SSI) evolution during the declining phase of the 23rd solar cycle have substantial implications for the modelling of the middle atmosphere evolution, leading not only to pronounced differences in the heating rates but also affecting photolysis rates. To estimate the role of SSI uncertainties we have compared oxygen (JO_2) and ozone (JO_3) photolysis rates calculated with the reference radiation code libRadtran using SSI for June 2004 and February 2009 obtained from two models (NRL, COSI) and one observation data set based on SORCE observations. We found that in the middle stratosphere changes in the photolysis rates for ozone can reach several tenths of % caused by the changes of the SSI in the Harley and Huggins bands for ozone and several % for oxygen caused by the changes of the SSI in the Herzberg continuum and Schumann-Runge bands. For the SORCE data set these changes are 2–4 times higher. We have also evaluated the ability of the several photolysis rates calculation methods widely used in atmospheric models to reproduce the absolute values of the photolysis rates and their response to the implied SSI changes. With some remarks all schemes show good results in the middle stratosphere compare to libRadtran. However, in the troposphere and mesosphere there are more noticeable differences.

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Rising of the 24th solar cycle

Cessateur Gaël¹, Adams Wilnelia^{1,2}, Schmutz Werner¹, Shapiro Alexander¹, Tagirov Rinat^{1,2}

¹ Physikalisches-Meteorologisches Observatorium Davos/ World Radiation Center, Davos, Switzerland

² ETH Zurich, Zurich, Switzerland

The main energy input to the terrestrial environment comes from solar radiation. The Sun varies on all time scales and its variability is strongly wavelength-dependent. At the same time, the mechanisms by which the solar irradiance and its variability might affect the various layers of the terrestrial atmosphere are still poorly known. For instance, various space weather applications, such as orbit determination, satellite communications, and positioning require a continuous and radiometrically calibrated monitoring of the solar spectral irradiance in the UltraViolet (UV). We will first briefly review the main mechanisms by which solar variability affects the Earth but also other planets.

We present also a new model of solar irradiance variability, CO-SIR for Code Of Solar Irradiance Reconstruction. Based on the assumption that the variability is triggered by the solar surface magnetism, we consider four types of active features such as sunspot umbra and penumbra, active network and faculae. The disc area coverages have been deduced from the segmentation of solar magnetograms and solar images as provided by the HMI instrument onboard Solar Dynamics Observatory. Spectra of active regions and the quiet Sun have been calculated with the radiative transfer code COSI. Model calculations are then directly compared with PREMOS observations in the UV and visible spectral ranges. Model and observations are in excellent agreement for rotational variability, longer-term variations being out of reach of the PREMOS instrument. We will also show that sunspots are not required to reconstruct the solar variability in the UV, while faculae play an important role in the visible.

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A new model for solar irradiance of the past and forecasts into the future

Adams Wilnelia, Schmutz Werner, Shapiro Alexander

Physikalisches-Meteorologisches Observatorium Davos/ World Radiation Center, Davos, Switzerland

Solar radiation is the main energy input to the terrestrial atmosphere, and thus determines the Earth's thermal balance and climate. A record of solar irradiance is required to assess the effects of irradiance variability on the climate of the past, the present and forecasts of future climate. Since direct observations of solar irradiance have only been available over the past three decades, we rely on models of irradiance over exceedingly longer timescales. The work presented here builds upon the approach by Shapiro et al. (2011). Since that publication, new observational and theoretical constraints have become available that necessitate a new approach to modelling irradiance variability.

Reconstructions of total solar irradiance (TSI) and solar spectral irradiance (SSI) are produced for the period 1800–2200. Our model treats the solar spectrum as an 11-year cyclic variation, associated with the sunspot cycle, superimposed upon a long-term trend. The model is tested against direct irradiance measurements for the satellite era. On timescales up to a few centuries, the model is based on proxies for irradiance variability. This set of proxies includes the 400-year sunspot record and concentrations of cosmogenic isotopes extracted from ice cores (^{10}Be) and tree rings (^{14}C). Predictions of TSI and SSI into the future rely on the length of these proxy records.

New implementations into the code include: addition of a penumbra contribution to the overall sunspot darkening effect on 11-year TSI variations; redistribution of sunspots (umbrae and penumbrae) and faculae into activity belts; the use of datasets of filling factors to calculate contrasts between umbra, penumbra and facular irradiance contributions.

Adjustment of the base model for the quiet sun is prompted by new solar and stellar data. The goal of this implementation is to improve the long-term trend over a multi-centennial timescale.

Analysis of nanoparticle-containing sunscreens with a miniaturized asymmetrical flow field-flow fractionation cartridge

Müller David^{1,2}, Calzolari Luigi³, Cattaneo Stefano¹, de Mello Andrew³

¹ Centre Suisse d'Electronique et de Microtechnique, Landquart, Switzerland

² Institute for Health and Consumer Protection, Joint Research Center (JRC) of the European Commission, Ispra, Italy

³ Department of Chemistry and Applied Biosciences, ETH Zurich, Switzerland

Asymmetrical flow field-flow fractionation (AF4) is a separation technique applicable to particles in a wide size range (1 nm – 100 µm). In current AF4 cartridges, a particle-containing liquid sample is injected into a long (~28 cm), narrow (~1 cm) and very shallow (~350 µm) channel. Depending on the various speeds by which differently sized particles move through the channel, the particles are being separated.

Despite the many advantages of AF4, its adoption for routine use is limited by the large size of currently available separation cartridges. The goal of this project was a miniaturization of the existing cartridge and its adoption to the analysis of complex nanoparticle-containing samples such as commercial sunscreens. The advantages of a cartridge scale-down include simplified handling, reduced costs, and higher throughput capacities.

A miniaturized AF4 cartridge was fabricated with a channel design similar to that used in larger FFF cartridges. By adapting the measurement protocols (application time and intensity of the various flows) to the new channel geometry, separation efficiencies comparable to conventional AF4 cartridges could be maintained, despite a channel length of less than 7 cm.

Initially, the setup was applied for the separation of a range of gold and silver nanoparticle mixtures (5 – 80 nm). After the initial characterization, we applied our platform to the analysis of commercial sunscreens containing TiO₂ nanoparticles. The analysis of nanoparticles in complex matrices and consumer products is a pressing problem that has to be faced by manufacturers, mainly due to newly enforced regulatory requirements (e.g. European Cosmetics Regulation). Those new requirements clearly call for cost-effective measurement systems to be operated in routine laboratories (e.g. QC lab of cosmetic production facility). In this context, the miniaturized AF4 cartridge could play a crucial role and help to promote FFF technologies in the everyday lab.

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Recreational activity in avalanche terrain: Influence of group size on avalanche risk

Procter Emily¹, Zweifel Benjamin², Boutellier Roman³, Strapazzon Giacomo¹, Staffler Hanspeter⁴

¹ Institute of Mountain Emergency Medicine, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italy

² WSL-Institute for Snow and Avalanche Research SLF, Davos, Switzerland

³ Technology and Innovation Management, ETH Zurich, Zurich, Switzerland

⁴ Abteilung Brand- und Zivilschutz, Bolzano, Italy

Avalanche prevention in the recreational sector has become more important due to increasing activity in winter backcountry terrain and corresponding number of annual avalanche accidents. Prevention initiatives have traditionally focused on physical factors such as snow cover, terrain or weather; however, more recently «prevention» also encompasses human factors such as decision-making strategies, group phenomena or heuristic traps. The value of different prevention measures has generally been based on expert consensus and not on a scientific approach to risk assessment due primarily to the lack of precise data and difficulty of realistic risk estimations. In this study, we analyze the risk of an avalanche involvement relative to group size, i.e. which group is most at risk when traveling in avalanche terrain. Compared to previous analyses, this is done for the first time by comparing the frequency of group sizes in winter backcountry recreationists (from in-field survey data) with the frequency of group sizes in

avalanche accidents statistics. The analysis includes transnational datasets from Davos, Switzerland (2004 to 2007, n=2299), and South Tyrol, Italy (2011, n=1927). The results are discussed against the background of established avalanche safety recommendations, the influence of a skier's load on snowpack and stability, and known group dynamics phenomena. The impact is a more representative estimation of actual frequency of group sizes and the correlation between group size and risk. Together with a basic understanding of group decision-making, recreationists and avalanche prevention initiatives can develop specific strategies to reduce risk.

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Field experiments on weak layer failure and crack propagation due to avalanche control by explosives

Simioni Stephan¹, Dual Jürg², Schweizer Jürg¹

¹ WSL-Institute for Snow and Avalanche Research SLF, Davos, Switzerland

² Department of Mechanical and Process Engineering, ETH Zurich, Zurich, Switzerland

Avalanche control by explosives is among the key temporary preventive measures and fixed avalanche control installations are frequently installed today. Hitherto, little is known about weak layer failure and crack propagation due to an explosion. In the winter 2013–2014 we performed a series of field experiments on a flat study site. We triggered slurry explosive charges ranging from 2.5 to 10 kg as used in avalanche control at different heights above the snow surface. At three different distances from the point of explosion we measured surface air pressure and accelerations within the snowpack at various depths. Cameras were placed in the snow pits for recording weak layer failure and crack propagation and to monitor the snowpack deformation by particle tracking velocimetry. We assessed whether weak layer failure occurred and if so whether it was caused by crack propagation or the direct impact of the air pressure wave above the point of observation (pit). We compared these results to the data recorded by the accelerometers and microphones to receive magnitudes required to cause weak layer failure in a given snowpack. The results show loading conditions required to fail a weak layer within a snowpack when using explosives. These findings might help to improve planning of avalanche control by explosives, in particular fixed avalanche control installations.

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Infection of Norway spruce by the pathogen *Chrysomyxa rhododendri*: Analysis of infection dynamics and establishment of resistant trees

Ganther Andrea^{1,2}, Mayr Stefan²

¹ alpS – Centre for Climate Change Adaptation, Innsbruck, Austria

² Institute of Botany, University of Innsbruck, Innsbruck, Austria

In the subalpine forests of the European Alps, Norway spruce (*Picea abies*) is frequently attacked by the rust fungus *Chrysomyxa rhododendri*. The parasite causes yellowing and defoliation of current-year needles and increases seedling dieback [1]. To counteract the difficulties in forest regeneration due to infections, we studied infection dynamics and the establishment of resistant saplings by vegetative propagation of naturally occurring resistant trees.

Spore flight was monitored over the season 2013 with a pollen trap in Praxmar (Tyrol, Austria) and correlated with climate parameters. The infection period was determined by a periodic application of the fungicide Mancozeb. In 2012, forty-five resistant trees were identified in Tyrol and reproduced together with 15 susceptible control trees by rooting of shoots in 2013: Twigs (n=5796) were harvested at the end of April and grown in a greenhouse gravel bed with controlled temperature and air humidity. After twelve weeks, rooted cuttings were transferred to pots.

Basidio spores were recorded from May to early July and aecio spores appeared from August to mid of October. High variation in spore-flight intensities between days was correlated with climate parameters. Needle infection occurred during three weeks (June,

19 to – July, 9). Rooting was successful for 18.9 ± 2.4 % of resistant and 5.8 ± 3.9 % of susceptible cuttings.

We conclude that (i) weather conditions are crucial for the pathogens' dispersal, whereby global warming may favour his spread. Needle infection was limited either by the end of spore flight or proceeded needle maturation. (ii) Clonal reproduction is a promising approach to establish resistant varieties. Resistance of all clones is currently tested by controlled infection with *C. rhododendri*. For the next years, the establishment of a resistant mother garden is planned providing plant material for future afforestations.

This research is financed by the alpS-COMET-projects B04 Adapt AF-C and L03 Adapt AF II (founded by BMVIT, BMFWF, Land Tirol, Land Vorarlberg and the company partners Landesforstgärten Tirol and Waldpflegeverein Tirol) and a scholarship from the «Südtiroler Assistentenverein».

[1] Ganthaler A., Bauer H., Gruber A., Mayr M., Oberhuber W., Mayr S. 2014. Eur J Forest Res 133, 201-211.

21

«Old» and «new» minorities: Perspectives on migration and identity in South Tyrol

Mitterhofer Johanna

Institute for Minority Rights, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italy

Migration policy aims to manage migration flows while guaranteeing the fundamental human rights of migrants and facilitating their inclusion in local society. In order to achieve this, migration policy needs to consider not only global or national developments, but also the socio-political, economic and cultural contexts at the regional and local level.

This presentation explores the relationship between migration policy and minority policy, and the opportunities and challenges that arise when migrants move to areas inhabited by minorities. It focuses on the Italian autonomous province of South Tyrol, characterized by the presence of two «historical» minorities (the German-speakers and the Ladins), the Italian-speaking population, and an increasing number of people with migration background – the so-called «new» minorities.

Within this pluriethnic context in which public resources and offices are divided neatly according to ethno-linguistic criteria, debates on migrant inclusion are closely tied to debates on its effects on the German-speaking and Ladin minorities. What are the effects of migration on the «traditional» ethno-linguistic composition of South Tyrol? Can, or should, minority rights be extended to «new» minorities?

Parallel to this concern on migration's impact on the status quo, there are calls to overcome the established ethno-linguistic divide. Instead of focusing on identity built on language and ethnicity, they promote a common «territorial identity», that is, an identity based on a sense of belonging to the same territory shared by all inhabitants of the region.

By exploring the various perspectives on the South Tyrolean migration policy debate and drawing on concrete case studies of initiatives promoting «territorial identity», this presentation provides insights into the complexity of migration debates applicable not just to South Tyrol, but to all contexts where multiple, and diverse, groups with «minority status» live side by side.

22

ID-Coop – Identity and cooperative enterprise in areas inhabited by linguistic minorities

Ellemunter Lisa

Institute for Minority Rights, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italy

Since the 1960s, the remote mountainous areas in the Alps have undergone demographic changes, albeit different in each case. Many of these areas are inhabited by linguistic minorities, whose mother tongue is the national language of the neighboring country (e.g., the Slovenes in Italy and Austria), or a proper own language (e.g., the Ladins in Italy). The areas addressed by the Interreg

Italy-Austria «ID-Coop» project (provinces of Belluno, Bolzano/Bozen, Udine, Gorizia in Italy, and the districts of Villach Land, Völkermarkt and Klagenfurt-Land in Austria) have recorded – and still record – asymmetric trends regarding linguistic and cultural identities, as well as demographic and economic developments due to several interlinked dynamics (e.g., various types of incentives to the local economy; disparities vis-à-vis the legal-institutional protection of groups and minorities).

In the frame of the International Year of Cooperatives launched by the United Nations for 2012, the potential of this form of economic, but also social (and cultural) enterprise from which benefit both its partners as well as the surrounding community, needs to be further explored.

Hence, the ID-Coop project aims to promote the cooperative enterprise as an economic resource for local linguistic minorities in order to enhance the sense of community and to offer a wide range of services in remote areas. By doing so, the project plans to promote a sustainable form of business that enhances awareness among the majority population about the cultural and economic added-value of minorities. The cooperative promoted by ID-Coop is also inspired by new forms of social enterprise (e.g., the European/cross-border cooperative; community-cooperatives created in the Reggiano Apennine). Indeed, the project focuses on the creation of a cooperative-model that will be concretely trialed in ID-Coop's disadvantaged areas.

This presentation thus aims to explore the role of cooperatives in promoting economic and social development in Alpine minority areas.

23

Balthasar Gioseph de Vincenz (1789–1858) und sein Meum Scret

Lutz Ursin^{1,2}

¹ Institut dal Dicziunari Rumantsch Grischun, Chur, Schweiz

² Universität Freiburg, Schweiz

Balthasar Gioseph de Vincenz wurde 1789 im surselvischen Siat geboren, wo er als Halbweise aufwuchs. Er entschied sich für eine Laufbahn als Söldner und schloss sich den Schweizerregimentern in Spanien an. Dort diente er von 1805 bis 1835.

In den Jahren 1817–1818 fasste er zudem den Plan, eine Bündner Kolonie in Spanien aufzubauen und er versuchte, diesen mit Hilfe der spanischen Behörden umzusetzen. Weiter leitete er die Bettelreise eines Disentiser Mönchs, der in Spanien Geld für das im Jahr 1799 von den Franzosen zerstörte Kloster sammeln sollte. Die Bündner Kolonie konnte nie realisiert werden und der Disentiser Pater mit den Einnahmen nur knapp seine Spesen decken. Beide Vorhaben scheiterten demnach kläglich.

Da sein Ansehen dadurch stark gelitten hatte, sah sich Vincenz nach seiner Rückkehr aus Spanien genötigt, unter dem Titel Meum Scret eine Verteidigungsschrift von rund 170 Seiten zu verfassen, um die Ursachen für das Scheitern der Pläne aus seiner Sicht darzulegen. Im Jahr 1858, kurz nach dem Verfassen seiner Handschrift, verstarb Vincenz in Disentis.

Diese surselvische Handschrift mit deutlicher spanischer Färbung ist eine Seltenheit für die rätoromanische Sprachwissenschaft. Jetzt wurde das Meum Scret erstmals eingehend bearbeitet, später wird es in Form einer kritischen Edition mit Glossar und Erläuterungen zum ersten Mal vollständig veröffentlicht werden.

Die Bedingungen für einen bündnerromanisch-spanischen Sprachkontakt werden nur selten erfüllt, es bedarf einer Biographie wie derjenigen von Vincenz. So streut der Autor in seinen surselvischen Text immer wieder spanische Wörter wie *limosna*, *potencia* ein, oder er formt spontane Wortkreuzungen wie *verdadeivel* «wahrhaftig» (surselv. *verdeivel* gekreuzt mit span. *verdadero*) oder *desventireivel* «unglücklich» (surselv. *sventireivel* gekreuzt mit span. *desventurado*). Darüber hinaus verwendet Vincenz zahlreiche Eigenheiten des spanischen Laut- und Schriftsystems. Sämtliche Sprachkontaktphänomene aus der Handschrift wurden gesammelt und in verschiedene Kategorien unterteilt.

Ein umfassendes Glossar, das nach heutigen lexikologischen Standards redigiert ist, erklärt sämtliche Wörter aus der Handschrift, die für den modernen surselvischen Leser nicht mehr oder nur schwer verständlich sind.

Wege des Gemeindedualismus. Eine Geschichte der Bündner Bürgergemeinden 1874–1974

Bundi Simon

Institut für Kulturforschung Graubünden, Chur, Schweiz

Am Institut für Kulturforschung läuft ein dreijähriges Forschungsprojekt zur Geschichte der Bürgergemeinden in Graubünden. Die je zur Hälfte vom Institut und vom Verband Bündnerischer Bürgergemeinden finanzierte Studie nimmt sich damit zum ersten Mal einem Thema an, das bislang in der neueren Geschichtsschreibung inexistent war. Die Vorstellung, dass die Ortsbürger das Gemeinwesen politisch allein leiten sollten, blieb in Graubünden bis in die 1870er-Jahre präsent. Bereits in den 1860er-Jahren erreichte der Anteil Niedergelassener in den Bündner Gemeinden indes ein Drittel der Gesamtbevölkerung, sodass eine Lösung dieser Spannung gefunden werden musste. 1874 legte dann ein neues Niederlassungsgesetz fest, dass den Ortsbürgern das alleinige Stimmrecht nur in einigen wenigen Angelegenheiten vorbehalten werde. Während bei kantonalen und eidgenössischen Wahlen und Abstimmungen bereits alle Schweizer das Stimmrecht hatten, versuchte der Kanton also, ein für jene Zeit demokratisch-egalitäres Modell der bürgerlichen Gesellschaft auch auf Gemeindeebene durchzusetzen.

Bis die Bündner Stimmbevölkerung im Jahre 1974 ein erstes Gemeindegesetz annahm, führte das Niederlassungsgesetz zu einem in der Schweiz beispiellosen Rechtskonflikt um den Status der verbliebenen Vorrechte der Ortsbürger. Dem Kanton gelang es nicht, eine Trennung zwischen Einwohner- und Bürgergemeinde zu vermeiden. Daran lässt sich zeigen, dass historisch fundierte Ideale wie die Gemeindeautonomie oder die republikanische Vorstellung einer auf das Gemeinwohl gerichteten Herrschaft tugendhafter Ortsbürger wirkmächtig blieben. Über Jahrzehnte wies der Bürgergemeinde-Diskurs zudem Ähnlichkeiten mit dem Heimatschutz auf, wurde doch hier wie dort mit dem Begriff des «Bodenständigen» argumentiert.

Es ist zudem interessant zu sehen, wo und ab wann sich in den meisten Gemeinden die organisatorische und statutarische Trennung von Einwohner- und Bürgergemeinde ausgebildet hat. Sehr oft folgten hier die regionalen Grenzen den Konfessionsgrenzen. Dieser Gemeindedualismus geschah jedoch nicht nur auf politischer Ebene, sondern ebenso im Verein, im Brauchtum und im täglichen Sprachgebrauch.

25

How safe is safe enough? A methodology for defining protection targets for critical infrastructures and services

Roth Andrea, Ammann Walter, Stal Marc

Global Risk Forum GRF Davos, Davos, Switzerland

Humans are increasingly dependent on technological advancements, which through their complexity and interdependence on other systems, increase the vulnerability of the overall society. Critical infrastructure systems like IT, transportation, energy supply, banking, food supply, health care systems, etc. are highly relevant for a well-being society, and failures may cause substantial losses. Security is closely linked to human activities. The technologies used «Too big to fail» and limited resources for securing the functionality of critical infrastructures are controversial facts that need a holistic approach for sustainable solutions. New and complex technologies, in combination with disastrous loss of life and assets, require an efficient and effective risk management approach to tackle the question: «How safe is safe enough?» Various risk management methodologies exist, but lack the essential element of setting protection targets, particularly for the collective risk of the society as a whole. The cost-benefit of protection mechanisms however, is a key factor for efficient and effective human safety and security. In addition, critical infrastructure operators on the one hand have to satisfy their shareholders, but have also and in particular a responsibility for providing the services in times of a crisis or a disaster. Society is heavily dependent on the functionality of critical infrastructures and services in times of a disaster (e.g. a hospital when an earthquake has occurred). Managing crises and disasters on a regional or even national level

must be able to rely on critical infrastructures. Their protection against disruption of vital functions therefore is crucial. The presentation will reflect on the limitations of existent approaches for protection targets (e.g. maximum permissible values, threshold values, etc.) before exploring a new methodology that sets standardized protection goals for collective risks based on a marginal cost approach, respectively the society's willingness to pay for a life saved. The methodology allows establishing an optimal amount of risk reduction and allows the comparability between the many different risks that have to be addressed within the context of a critical infrastructure. Finally, the presentation will also discuss the tolerable limits for the individual risks.

26

Reliability analyses provide guidance to cost-efficient early warning systems for natural hazards

Sättele Martina¹, Bründl Michael¹, Straub Daniel²

¹ Avalanche Dynamics and Risk Management, WSL-Institute for Snow and Avalanche Research SLF, Davos Dorf, Switzerland

² Engineering Risk Analysis Group, Technische Universität München, Munich, Germany

Gravitationally driven natural hazard processes have been threatening persons and infrastructure in alpine regions for decades. Early warning systems (EWS) are increasingly applied as preventive risk mitigation measures that detect hazard events in an early stage and allow safety personnel to take intervention measures. While the versatility and technical performance of EWS are constantly increasing, their effect on risk has rarely been investigated. Within the Project ReWarn we classify EWS into two main types (1. warning; 2. alarm systems) and assess the effect on risk reduction in case studies. In a guideline, we summarize the factors which largely influence the system performance. We consider both the technical and the inherent reliability. The technical reliability of both system types is closely related to failure probabilities of individual system components and the system configuration. Redundancies and multi-level-monitoring approaches drastically increase the system performance, while dependencies between the components have a negative influence on the technical availability of the system. The effect on risk reduction due to the factors that are summarized by the term «inherent reliability» is significantly higher. The ability of alarm systems to distinguish between hazard and noise and take successful intervention measures relies on the predefined threshold and the compliance of endangered people to the alarm. For warning systems, the quality of available sensor data, models and human decision-making are determinant factors for the success of intervention. In the guideline, we structure our main findings in a comprehensive document to support the development and operation of cost-efficient EWS.

27

Participatory mapping: A tool for participatory policy development in protected areas

Rohrbach Benjamin

Department of Geography, GIScience Unit, University of Zurich, Zurich, Switzerland

In this PhD-Thesis, we investigate participatory mapping as a tool to facilitate spatial planning. In our approach, recent aerial photos serve as a basis for the mapping. Participants then contribute by drawing areas on top of the orthophotomap. As an example, we investigate the agricultural policy development in the val Müstair, a biosphere reserve in the Swiss mountains. There, the area used for arable farming decreased by over 50% from 1990 to 2010. Literature shows, that arable farming contributes to various ecosystem services, such as cultural heritage, education, knowledge systems, genetic resources, and aesthetic landscapes. At the same time, it draws on those services. In the future, -upon request of the local stakeholders- Swiss agricultural policy subsidizes arable farming in the mountains. We now investigate the question: Which sites would most probably be used for arable farming and, do they fit into the overall management plan of the biosphere reserve?

For our participatory mapping exercise, various stakeholders marked potential arable farming areas on the orthophotomaps. We asked 17 farmers to mark areas likely to be used for arable farming in the near future, and to talk about the importance of arable farming for the landscape, as well as the preservation of plant genetic resources in the area. We thus draw a more complete picture of possible policy measures to increase and the provision of multiple ecosystem services.

28 Der Alpenraum als Labor der grenzüberschreitenden Zusammenarbeit: Der EVTZ «Europaregion Tirol-Südtirol-Trentino» und die makroregionale Strategie für die Alpen

Klotz Greta¹, Trettel Martina^{1,2}

¹ Institut für Föderalismus- und Regionalismusforschung, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italien

² Università degli studi di Verona, Italien

Mit dem Vertrag von Lissabon wurde zu den Grundsätzen der sozialen und wirtschaftlichen Kohäsion zwischen den EU Mitgliedsstaaten ein dritter Aspekt hinzugefügt: Der territoriale Zusammenhalt. Verankert wurde dieses Ziel durch Artikel 3 des Vertrages über die Europäische Union (EUV) und Artikel 174 des Vertrages über die Arbeitsweise der Europäischen Union (AEUV). Um dieses Ziel zu verwirklichen hat die EU, zum einen mit der Verordnung Nr. 1082/2006 das rechtliche Instrument des «Europäischen Verbunds für territoriale Zusammenarbeit» (EVTZ) geschaffen, das die grenzüberschreitende Zusammenarbeit zwischen territorialen Gebietskörperschaften ermöglichen soll. Zum anderen wurde mit der makroregionalen Strategie (MRS) für den Ostseeraum im Jahr 2009 erstmal eine neue Form der europäischen transnationalen Kooperation eingeführt, mit dessen Hilfe staatsübergreifende Herausforderungen eines bestimmten geografischen Gebiets gemeinsam koordiniert werden sollen. Beide Konzepte – EVTZ und MRS – basieren auf der Grundidee, die territoriale und grenzüberschreitende Zusammenarbeit zwischen lokalen, regionalen und nationalen Gebietskörperschaften und Akteuren zu unterstützen. Trotz dieser Gemeinsamkeit, unterscheiden sich die Konzepte in Form, Struktur und Inhalt maßgeblich. Während es sich bei der MRS um ein politisches integriertes Rahmenkonzept ohne eigene finanzielle Mittel handelt, basiert das Instrument des EVTZ auf einer stabilen rechtlichen Grundlage.

Für diese beiden Formen der grenzüberschreitenden Zusammenarbeit bietet sich der Alpenraum, ein geografisches Grossgebiet im Herzen Europas, welches durch das Gebirge der Alpen acht Staaten miteinander vernetzt, als interessantes praktisches Beispiel an. Die Länder und Regionen im Alpenbogen stehen durch die Alpen als verbindendes Element zunehmend vor gemeinsamen Herausforderungen: Der Alpenraum eignet sich daher bestens, grenzüberschreitende Instrumente und Strategien zu erproben.

Die beiden grenzüberschreitenden Konzepte der EU – der EVTZ und die makroregionale Strategie – werden daher am Beispiel des EVTZ «Europaregion Tirol-Südtirol-Trentino» und der geplanten makroregionalen Strategie für den Alpenraum untersucht, um den Alpenbogen als Labor der grenzüberschreitenden Zusammenarbeit vorzustellen.

29 Patienten mit einem Bronchuskarzinom auf einer Palliativstation – Eine prospektive Studie über die Symptome und deren Behandlung

Camartin Cristian¹, Kuhn Max²

¹ Palliative Care, Kantonsspital Graubünden, Chur, Schweiz

² Pneumologie, Kantonsspital Graubünden, Chur, Schweiz

Einleitung: In der Schweiz ist das Bronchuskarzinom der häufigste Tumor bei Männern und der zweithäufigste Tumor bei Frauen. Auf unserer Palliativstation beträgt der Anteil von Patienten mit einem pulmonalen oder pleuralen Tumor 25.7% aller Zuweisungen und stellt so die größte Patientenpopulation dar. Die Morbidität und Mortalität dieser Patienten ist sehr hoch.

Material und Methode: In dieser prospektiven Studie haben wir vom 1. November 2012 bis zum 31. Oktober 2013 die Beschwerden aller Patienten mit einem pulmonalen und pleuralen Tumor erfasst. Täglich wurden Dyspnoe, Husten, störende Schleimproduktion, Schmerzen, Hämoptoe, Appetitlosigkeit, Depression, Schlafprobleme, Fatigue, Suizidgedanken, Nebenwirkungen der Tumortherapie, soziale und familiäre Probleme aufgezeichnet und auf einer visuellen Analogskala in fünf Schweregrade eingeordnet. Eine standardisierte Therapie wurde gemäß internationalen Empfehlungen durchgeführt.

Ergebnisse: Insgesamt wurden 52 Patienten erfasst. Alle Patienten haben eine Vielzahl von Beschwerden angegeben. Die häufigsten Beschwerden waren Appetitverlust, Fatigue, Schmerzen und Dyspnoe. Die Dyspnoe war das Symptom mit der subjektiv stärksten Belastung. Bei den entlassenen Patienten konnte eine signifikante Verbesserung der Dyspnoe und der Schmerzen beobachtet werden. Die übrigen Symptome konnten kaum beeinflusst werden.

Während des Aufenthaltes sind 56% der Patienten verstorben. Der Wunsch einer Suizidbeihilfe wurde nie ausgesprochen.

Folgerung: Pulmonale und pleurale Tumoren sind häufige Tumoren auf Palliativstationen. Morbidität und Mortalität sind sehr hoch. Vorherrschende Symptome sind Appetitlosigkeit und Fatigue. Eine erfolgreiche Behandlung der belastenden Symptome Dyspnoe und Schmerzen ist mit einer standardisierten Therapie möglich. Suizidgedanken werden selten ausgedrückt.

30 Results and postoperative quality of life in patients greater than 80 years old after colorectal surgery

Schraffl Daniel, Joos Renzo, Villiger Peter

Departement of Surgery, Kantonsspital Graubünden, Chur, Switzerland

Background: There are several challenges in surgical treatment of colorectal diseases in patients over 80. Our goal was to determine outcomes after colorectal surgery with postoperative quality of life [evaluated according to SF-36] and mortality.

Methods: This study includes postoperative colorectal surgery patients over 80 years between January 1, 2009 and December 31, 2013. Data was taken from our hospital database, general practitioner' and patients' interviews. We included curative and palliative as well as elective and emergency interventions.

Results: One hundred and seven patients (46 male, 61 female, age between 80 and 99 years, mean age 87.2 +/- 5 years) were studied. Median follow up was 29 months. Five patients were lost to follow up. The overall mortality rate was 39.2 %. The 30-day mortality rate of all patients was 13 %. Ten of 14 patients that died within the first 30 days had an emergency surgery. Based on SF-36 results, most of surviving patients had an improvement in postoperative quality of life. Patients without benefit most often claimed aggravation of pre-existing defecation problems. The correlation between ASA score and functional renal impairment mortality was highest in first 30 days.

Conclusion: Operation in patients over 80 years is safe. Emergency surgery has a much higher mortality rate than elective surgery. Risk factors include a high ASA score and functional renal impairment. Postoperative survivors demonstrated superior SF-36 scores and improved quality of life.

31 Preventive/therapeutic vaccines in a murine model of allergy

Prati Moira, Cramer Reto, Ferstl Ruth, Frei Remo, Garbani Matia, Rhyner Claudio

Swiss Institute for Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

Objective: The incidence of IgE-mediated diseases in industrialized countries is still increasing and it is therefore of paramount importance to develop new therapeutic approaches for the prevention and/or efficient therapy of allergic diseases. Methods: Our research activities aim at providing strategies to control or permanently suppress IgE mediated hyper-reactivity reactions.

Two main approaches have been considered during this study, i) blocking the interaction of IgE with the Fc ϵ Receptor by constitutive inhibition of sIgE, and ii) suppress new IgE responses by depleting IgE⁺ memory B cells by extracellular targeting of the membrane-bound IgE as part of the B-cell receptor (BCR). The approach to target soluble and membrane-bound IgE is based on direct targeting of the MHC class-II antigen presentation pathway with the help of modular antigen translocation (MAT) constructs. These were tested in an in vivo murine model of allergy to demonstrate that humoral immune responses against self antigens can be elicited.

Results: Preliminary results show induction of protective IgG2a antibody responses, and a reduction of serum IgE levels as well as B cell numbers in the blood and spleen. Significant decrease in BAL cells, and eosinophil counts in particular, were also observed after vaccination. In the near future, the MAT-vaccines will be tested in a prophylactic in vivo murine model of allergy or asthma.

Conclusions: These vaccination strategies principally aim at providing a long-lasting protection. Improvement in this context could represent a benefit for allergic patients eliminating the need for symptomatic treatments and increasing their quality of life. Moreover, MAT-vaccines could open a new therapeutic opportunity to cure allergic diseases in a short time, representing a promising strategy to improve the development of potent allergy vaccines.

32

Parametric analysis of proximal femur morphology on fracture behavior in sideways fall situations

Voegtli Daniela, Kamer Lukas, Noser Hansrudi, Widmer Daniel, Windolf Markus

Biomedical Services, AO Research Institute, Davos, Switzerland

Background: In the elderly population, femoral fractures are a major concern in traumatology due to osteoporotic bone occurrence. The aim of this study was to investigate with numerical models how specific bone morphological parameters, such as bone density or size, influence the fracture risk at the proximal femur.

Methods: The AO Research Institute proposed an averaging technique for numerical generation of statistical bone shapes and density maps from a cohort of CT-scanned human femora. In the scope of this project, several morphological parameters were identified as most important indicators for fracture occurrence. A set of statistical bone models was numerically generated representing extreme variations of the named parameters. The models were then transferred into a finite element (FE) environment and virtually tested in a simulated sideways fall using non-linear FE analysis. The models had been designed according to an established mechanical free fall test setup¹. Validation of the developed numerical models was performed with biomechanical tests on fresh-frozen human cadaveric bones. Existing mechanical and virtual models were enhanced with additional simulation of the soft tissue mantle lateral to the greater trochanter to better mimic load transfer between bone and ground.

Results: Identified parameters most influential for fracture risk of the proximal femur were bone density, neck width, and length as well as CCD angle. Numerical simulations revealed distinct differences with regard to the named parameters related to energy uptake, maximal failure load and stiffness. Computer simulations showed good correlations to the reference tests on cadaveric bone.

Conclusion: A systematic understanding of the effect of bone morphology on the individual fracture risk can help to identify high-risk patients to reduce the incidence of hip fractures in the future.

Reference List: (1) Fliri, L., et al., Limited V-shaped cement augmentation of the proximal femur to prevent secondary hip fractures. *J Biomater Appl*, 2013. 28(1): p. 136–43.

POSTER PRESENTATIONS

P1

A comprehensive radiation flux assessment at different sites in Switzerland

Aebi Christine^{1,2}, Groebner Julian¹, Kaempfer Niklaus²

¹ Physikalisches-Meteorologisches Observatorium Davos/World Radiation Center, Davos, Switzerland

² University of Bern, Bern, Switzerland

Radiative transfer calculations in the atmosphere and the influence of clouds on the radiation budget remain the greatest sources of uncertainty in the simulation of climate change. Lack of global quantitative surface measurements of radiation, the shortage of high quality satellite and surface-based observational records, inhomogeneities in the data and insufficient precision in measurements of small changes in cloudiness and radiation, which can have large impacts on the Earth's climate, are reasons for the aforementioned uncertainties. Consequently, in order to assess the radiative impact of clouds on the radiation budget and the corresponding changes, frequent and more precise radiation and cloud observations are necessary.

The focus of this project is on the measurement and analysis of specific radiation processes at selected sites in Switzerland. The combination of surface-based radiation flux measurements with radiative transfer calculations will allow a complete assimilation and closure study to be performed on the surface radiation budget at four different sites in Switzerland (Davos, Jungfrauoch, Locarno-Monti, and Payerne). At these different sites, the role of clouds and aerosols on longwave and shortwave surface radiation fluxes will be studied. Studies for clear-sky conditions have shown a high level of agreement between model calculations and measurements. Thus, the focus of this project is to analyse the radiation budget under overcast and broken cloud situations.

Visible all-sky camera systems in Davos, Jungfrauoch and Payerne detect and classify clouds on an automatic basis. In order to complement these measurements during the day, a thermal infrared all-sky camera system for night-time operation will be developed. By this means, the dependence of cloud radiative forcing on atmospheric composition and cloud type can be quantified. This study will be complemented by an assessment of measured and modeled radiation fluxes at the GCOS Reference Upper-Air Network (GRUAN) and the Baseline Surface Radiation Network (BSRN) station in Payerne, which hosts a large amount of remote-sensing instrumentation, to determine the atmospheric state. Another part of the project focuses on the homogenisation and analysis of the 20-year long data set (1996–2016) of shortwave and longwave data fluxes at the four Swiss Alpine Climate and Radiation Monitoring (SACRAM) sites in Switzerland. This data set aims at determining the ongoing long-term changes of these components.

P2

Remote and terrestrial ground monitoring techniques integration for hazard assessment in mountain areas

Chinellato Giulia¹, Iasio Christian¹, Kenner Robert², Mair Volkmar³, Mosna David³, Mulas Marco^{1,4}, Phillips Marcia², Strada Claudia³, Zischg Andreas⁵

¹ Institute for Applied Remote Sensing, European Academy of Bozen/Bolzano (EURAC), Bolzano, Italy

² WSL-Institut für Schnee- und Lawinenforschung SLF, Davos, Switzerland

³ Amt für Geologie und Baustoffprüfung, Bolzano, Italy

⁴ Department of Chemistry and Earth Science, University of Modena and Reggio Emilia, Modena, Italy

⁵ Aabenig AG, Chur, Switzerland

In high mountain regions the choice of appropriate sites for infrastructure such as roads, railways, cable cars or hydropower dams is often very limited. The new role played by the precautionary monitoring in the risk governance becomes fundamental and may overcome the modeling of future events, which represented so far the predominant approach to these sort of issues. The scale factor of the observed area and the multiple purpose

of such regional ordinary surveys make it convenient to adopt Radar Satellite-based systems, but they need to be integrated with terrestrial systems for validation and eventual early warning purposes. Significant progress over the past decade in Remote Sensing (RS), Proximal Sensing and integration-based sensor networks systems now provide technologies, that allow to implement monitoring systems for ordinary surveys of extensive areas or regions, which are affected by active natural processes and slope instability. The Interreg project SloMove aims to provide solutions for such challenges and focuses on using remote sensing monitoring techniques for the monitoring of mass movements in two test sites, in South Tyrol (Italy) and in the Canton of Grisons (Switzerland). The topics faced, concern mass movements and slope deformation monitoring techniques, focusing mainly on the integration of multi-temporal interferometry, new generation of terrestrial technologies for differential digital terrain model elaboration provided by laser scanner (TLS), and GNSS-based topographic surveys, which are used not only for validation purpose, but also for adding value and information to the whole monitoring survey. The test sites are currently observed by an integrated monitoring design that includes reference targets for the different monitoring systems placed together on the same point or rigid foundation, to facilitate the comparison of the data and to be able to switch consistently from one to the other system.

P3

WIKIALps: A wiki for capitalizing on spatial-development projects

Cortines Felipe¹, Brozzi Riccardo², Pecher Caroline¹, Tappeiner Ulrike¹

¹ Institute for Alpine Environment, European Academy of Bozen/Bolzano (EURAC), Bozen, Italy

² Institute for Regional Development and Location Management, European Academy of Bozen/Bolzano (EURAC), Bozen, Italy

Spatial development is a crucial issue in the Alpine Space where economy, society, and environment have to coexist in a very confined space. Any small action taken in any of these fields can trigger big alterations in the others. In the same way, actions taken at local, regional or national level have consequences that affect other countries within the Alpine Space.

A balanced and shared territorial development in all the Alpine Space countries needs appropriate, current and manageable information for a sound decision-making. Nowadays the big and diverse amount of information available makes finding the correct and useful pieces very difficult and time consuming. The WIKIALps project provides operative ready-to-use tools to facilitate decision makers, civil servants, researchers, and entrepreneurs on this task.

The project capitalises on Alpine Space program projects from two thematic fields, «Inclusive growth» and «Resource efficiency and ecosystem management», thus highlighting: not recognized synergies, remaining gaps, achievements that could be further implemented, emerging contradictions, potential requirements and benefits for sustainable transnational spatial development.

To obtain a multidisciplinary overall picture of spatial development in the Alpine Space, WIKIALps analyses it from three different angles. 1) The tools available through the results of selected Alpine Space projects. 2) The actors involved, through a stakeholders analysis. And 3), the challenges and needs through relevant spatial development documents at the regional, national and international level, and conversations with stakeholders.

All the results are linked together in WIKIALps, a wikipedia like information platform on spatial development. This wiki will help with the daily work of the people steering spatial development in the Alpine Space. In addition, it serves as an innovative pilot experience on how to capitalise on project results.

The project WIKIALps is co-financed by the European Regional Development Fund in the frame of the European Territorial Cooperation Programme Alpine Space (www.alpine-space.eu).

P4

Solar variability and climate change during the first half of the 20th century (SOVAC)

Egorova Tatiana¹, Rozanov Eugene^{1,2}, Werner Schmutz¹

¹ Physikalisches-Meteorologisches Observatorium Davos/World Radiation Center, Davos, Switzerland

² Institute for Atmospheric and Climate Science, ETH Zurich, Zurich, Switzerland

In the SOVAC project we study the causes of observed climate warming during the first half of the 20th century. To address this question we will simulate the climate evolution from 1880 to 1950 using our atmosphere-ocean-chemistry-climate model (AOCCM) SOCOL-MPIOM and the updated reconstructions of all known climate forcings. Most of the models that participated in the IPCC AR4 experiment failed to reproduce statistically significant global warming as well as typical features of its space pattern like e.g., the warming over the continental US and over the Arctic. This problem remains important and should be re-investigated given the noticeable recent progress in modeling and understanding of past solar irradiance variations. The problem will be addressed with a series of multi-year ensemble runs of the AOCCM SOCOL-MPIOM driven by all known anthropogenic and natural forcings taken in different combinations to elucidate the effects of anthropogenic factors as well as natural phenomena such as solar spectral irradiance, energetic particle precipitation and volcanic aerosol loading. The seasonal and geographical patterns of the climate change during the considered period will be compared to observational data and reanalysis products to establish the robustness of the obtained climate behavior. The analysis of the sensitivity runs will allow disentangling the contribution of different forcing mechanisms which are responsible for climate change. The results will have implications for the forecast of future climate change due to the combined effects of anthropogenic and natural factors.

P5

The role of small scale heating events in the coronal heating

Guerreiro Nuno¹, Haberreiter Margit¹, Hansteen Viggo², Schmutz Werner¹

¹ Physikalisches-Meteorologisches Institut Davos/ World Radiation Center, Davos, Switzerland

² Institute of theoretical astrophysics, Oslo, Norway

Levine (1974) first suggested the coronal heating problem could be explained by a multitude of small reconnection events. Parker (1988) built up on Levine's idea and first introduced the term *nanoflare*. Nanoflares are considered to have an average energy of 10^{24} erg. In order for them to significantly contribute to the heating of the corona the current understanding is that they have to follow the energy distribution, $dN/dt \sim E^{-\alpha}$, with α being larger than 2. However, with the low energy they release, nanoflares lie below the limit of detectability with current state-of-the-art space instrumentation. Therefore, we focus on the analysis of existing 3D MHD simulation, which offer the unique possibility to study small scale heating events that maintain the continuous heating of the corona. We present a technique for the identification and characterization of the small heating scale events from these simulations. Moreover, we calculate the energy distribution of the heating events and finally determine their contribution to the coronal heating.

P6

On the potential of a novel avalanche radar system

Köhler Anselm¹, Ash Matthew², Brennan Paul², Keylock Chris³, McElwaine Jim⁴, Sovilla Betty¹

¹ WSL-Institute for Snow and Avalanche Research SLF, Davos, Switzerland

² University College London, London, United Kingdom

³ University of Sheffield, Sheffield, United Kingdom

⁴ Durham University, Durham, United Kingdom

Avalanches are a common geophysical flow phenomenon in snow covered mountainous regions. As a consequence of their significant impacts on infrastructure, economy and tourism in densely settled areas, the physical understanding of avalanche flows is very important for risk management and the design of defensive structures. Today the physics of avalanches is still poorly understood due to their complicated nature as well as the lack of data with high spatial and temporal resolution.

We have developed a radar system that is installed at the Vallée de la Sionne avalanche test site in the Canton Wallis. The radar can monitor avalanches with unprecedented spatial and temporal resolution. The range gate resolution of around one meter downslope is sampled every 10 milliseconds. Furthermore, the radar has the capability to detect lateral positions of the avalanche flow as well as intrinsic Doppler velocities. Since the installation in 2010, we were able to record around 40 naturally occurring avalanche events.

To show the potential of this radar system we present data from a small wet snow avalanche that typically occurs in spring season. The data set shows different flow structures such as separated fronts, trackable large granules, and surge overrunning in the deceleration phase. We extract these features and combine them with other measurements and numerical modeling to gain a comprehensive image of this particular avalanche with unprecedented definition.

P7

Electrochemical microsensors for monitoring the functions of liver cells in a modular based microfluidic system

La Cour Jakob Bonne^{1,2}, Barbe Laurent¹, Generelli Silvia¹, Guenat Olivier^{1,2}

¹ Centre Suisse d'Electronique et de Microtechnique, Landquart, Switzerland

² ARTORG Center, University of Bern, Bern, Switzerland

European legislation is restricting the use of animals for toxicological studies, which increases the need for alternative testing methods. The HEMIBIO project aims at developing a hepatic 3D microbio reactor reproducing the complexity of the liver for pre-clinical toxicity testing. One of the major challenges in building a 3D-liver bioreactor is the lack of data on the complex environment present inside the bioreactor where the cells live, aggregate and differentiate. Most of the time, physiological samples are aliquoted to determine hepatic functions and metabolism, which is an inaccurate, time-consuming and often destructive process in particular when the sample volumes are small. In these circumstances, microsensors located in the direct vicinity of the cells can play a vital role, by monitoring cell culture conditions and thus help mimic the natural microenvironment.

In order to simplify the overall structure of the microbio reactor, independent modules for cell culture and sensing will be integrated. Our specific objective is to develop one of the microsensors modules that will integrate an alanin-aminotransferase (ALT), a urea and a NH₄⁺ electrochemical microsensors. These microsensors will be interrogated at specific times (for instance after a toxic insult) and will provide crucial information related to the current cell conditions. The modular concept will not only allow for replacement of faulty sensors during cell cultivation if needed, but also to implement additional sensors able to discriminate the specific patterns of liver injury (cholestasis, steatosis).

ALT, urea and NH₄⁺ have been chosen as highly specific markers of liver cell metabolism.

P8

Simulation of snow stratigraphy using full-waveform inversion applied to data from an upward-looking radar system

Schmid Lino¹, Eisen Olaf^{2,3}, Heilig Achim^{2,3,4}, Maurer Hansruedi⁵, Mitterer Christoph¹, Schweizer Jürg¹, Okorn Robert⁶

¹ WSL-Institute for Snow and Avalanche Research SLF, Davos, Switzerland

² Institute of Environmental Physics, University of Heidelberg, Heidelberg, Germany

³ Alfred Wegener Institute for Polar and Marine Research AWI, Bremerhaven, Germany

⁴ Department of Geosciences CGISS, Boise State University, Boise (ID), USA

⁵ Institute of Geophysics, ETH Zurich, Zurich, Switzerland

⁶ Electronic & Technology Management (ETM), FH JOANNEUM, Kapfenberg, Austria

Snow stratigraphy is a key contributing factor for assessing avalanche danger, but so far only destructive methods can provide this kind of information. Furthermore, continuous monitoring of the temporal evolution of the snowpack is not possible with destructive methods. Radar technology provides information on the snowpack non-destructively and allows deriving internal snow properties. In our previous work, we demonstrated that it is feasible to quantitatively derive snowpack properties relevant for avalanche formation and monitor their evolution in time using an upward-looking ground penetrating radar system (upGPR) that was buried in a wooden box underneath the snow. Reliable results could only be obtained for the time when the snow cover was dry. In addition, to determine some properties, we still needed additional information such as independently measured snow height or modeled snow density. Hence, the system was not yet able to provide information from avalanche starting zones, since this type of information is generally not available in avalanche-prone terrain. To fully exploit the information content of upGPR data, and thus to at least partially compensate for the lack of information we applied full-waveform inversion (FWI) techniques. We refined the model of the snowpack by repeated forward modeling of the waveforms and updating the model parameters to match it with recorded data. The forward model took into account both the effect of the snow density on the velocity of the electromagnetic wave, as well as the influence of snow wetness on the attenuation. This allowed the density and the liquid water content for each layer in the snowpack to be determined. As we conducted a measurement every 3 hours (every 30 minutes as soon as the snowpack became wet), we could also simulate the temporal evolution of the density and the liquid water profiles. The method worked without assumptions or external measurements.

P9

Granulation of snow: Experiments and discrete element modeling

Steinkogler Walter^{1,2}, Gaume Johan¹, Lehning Michael^{1,2}, Löwe Henning¹, Sovilla Betty¹

¹ WSL-Institute for Snow and Avalanche Research SLF, Davos, Switzerland

² CRYOS, School of Architecture, Civil and Environmental Engineering, EPFL, Lausanne, Switzerland

The flow dynamics of snow avalanches can strongly differ for individual avalanches even if the release conditions are similar. The development of different flow regimes, e.g. whether a plug flow or a sheared flow is formed, strongly depends on the snow properties in the avalanche. Depending on whether the avalanche was dry, moist or wet, typical granular structures and size distributions can be observed in the deposition zone. These are then often interpreted as indirect indicators of the internal flow dynamics of an avalanche. In order to understand under which circumstances granules form, we used a concrete tumbler to examine the granulation, the generic name for particle size enlargement, of snow with different properties. Our experiments show that granulation of snow only occurred when a snow temperature of -1°C was exceeded. No granule formation could be observed below this temperature threshold. To better understand the physical processes

involved in the granule formation, cohesive discrete element simulations were performed, allowing to correctly reproduce the size distributions of dry, moist and wet granules as measured in the tumbler and real-scale avalanches. The results of this paper confirm recent studies that the snow temperature plays a crucial role on granulation and thus on the flow dynamics of avalanches since it may strongly change the structure of the flowing snow. This investigation provides a first step for more complex and real-scale modeling of flowing cohesive avalanches and shows that granulation has the potential to link snow cover properties with avalanche dynamics.

P10

Measurements of the Total Solar Irradiance

Suter Markus, Finsterle Wolfgang

Physikalisch-Meteorologisches Observatorium/ World Radiation Center, Davos, Switzerland

Total Solar Irradiance (TSI) is a key input parameter for the climate on earth. Constant monitoring as well as knowledge on the absolute value of TSI is therefore crucial for understanding and forecasting our climate.

The Physikalisch-Meteorologisches Observatorium Davos and World Radiation Center (PMOD/WRC) has a long time experience in building radiometers to measure TSI. Starting in 2009 a new prototype instrument for satellite based measurements, the Digital Absolute Radiometer (DARA) had been developed. DARA type radiometers will reduce the uncertainty of absolute TSI values significantly, compared to previously operated PMO6 radiometers. Future applications of these new instruments are the CLARA instrument on the NORsat-1 satellite and the SUMO instrument on the PROBA-III satellite.

In radiometry different irradiance standards, such as the World Radiometric Reference (WRR) or the SI cryogenic laboratory standard, have been used to calibrate radiometers. Implementations of different standards have led to much confusion in the past. Also, the recent discussion on the «true solar constant» is eventually a question of using the «right» scale.

DARA type radiometers will have a native scale implemented that is directly linked to the SI base units and therefore independent of irradiance standards. Thus, DARA is fully characterised in order to measure solar irradiance in SI units (W/m^2). This characterisation includes several experiments as well as theoretical work to characterise side effects that bias the measurement and improve the understanding of these effects.

DARA has been tested and characterised in detail during the last four years. We will discuss the realisation of the instruments native irradiance scale and its uncertainties. Furthermore, the general performance of DARA and the results from comparisons of DARA to reference instruments and reference standards (WRR/ SI cryogenic laboratory standard) will be discussed.

P11

Fast non-LTE radiative transfer numerical scheme for solar spectrum modeling

Tagirov Rinat, Schmutz Werner, Shapiro Alexander

Physikalisch-Meteorologisches Observatorium Davos/ World Radiation Center, Davos, Switzerland

We have been working on the implementation of a fast and reliable non-LTE radiative transfer numerical scheme within COde for Solar Irradiance (COSI) that was developed at the Physical Meteorological Observatory Davos (PMOD) for solar spectrum modeling.

Briefly, a non-LTE radiative transfer problem in a stellar atmosphere can be described by two equations: the radiative transfer equation and the statistical equilibrium equation. The latter (being actually a system of equations) given the intensity of radiation at each atmospheric depth point yields the populations of all atomic levels included in the calculations. The former having these atomic populations as an input gives the intensity of radiation. In the case of the problem in question, these equations are interconnected in a nonlocal and nonlinear way making it im-

possible to solve the problem analytically. The numerical way to solve it is by means of iterating between these two equations. In numerical schemes the equation of radiative transfer is written in operator form resulting in only one matrix describing the radiative transfer. This matrix is called Λ -operator (LO). Hence the aforementioned iterations are referred to as Λ -iterations.

Unfortunately Λ -iterations have a property of stabilizing long before the correct solution is reached in atmospheric regions where optical depth for a given photon frequency is large and therefore such a straightforward approach cannot be used. To circumvent this behavior one has to implement the Accelerated Λ -Iterations (ALI) - a technique in which LO is split in two parts, one of which is called an approximate Λ -operator (ALO) and is used to accelerate the convergence of Λ -Iterations. ALO can take any form as long as it is easily invertible and serves as a good physical approximation to the initial LO. This gives a lot of freedom in ways to choose ALO and therefore many different approaches have been proposed for a variety of radiative transfer problems in the Sun and other stars. The goal of this project has been to employ the so-called local ALO in the ALI scheme within COSI.

COSI solves the radiative transfer in the Sun within the co-moving system of reference framework (one allowing for a possible expansion of the atmosphere). To our knowledge, the local ALO has never been implemented before in the co-moving system of reference. Accomplishment of our objective expanded the computational capabilities of COSI. Namely, such new capabilities, among others, include proper calculation of the emergent intensity in the Ly α line and in the radio continuum (0.1 mm – 30 cm), both of which are crucial for a number of parallel and future projects to be carried out at PMOD.

P12

Modeling of winter terrain surface to improve avalanche release zone estimation

Veitinger Jochen¹, Purves Ross², Sovilla Betty¹

¹ WSL-Institute for Snow and Avalanche Research SLF, Davos, Switzerland

² Department of Geography, University of Zurich, Zurich, Switzerland

Location and extent of avalanche starting zones are of crucial importance to correctly estimate the potential danger that avalanches pose to roads, railways, or infrastructure. They are also an important input parameter in avalanche dynamics modeling, as they determine together with fracture depth the initial volume of an avalanche. One difficulty to estimate avalanche release areas is that they vary in location and size within the same topographical basin due to different snow cover distribution. During the accumulation season of snow, terrain features successively disappear leading to more homogeneous deposition patterns and thus to a progressive smoothing of the terrain surface. These changing deposition patterns might partly explain the differences in release areas.

We present a new GIS based tool that estimates potential release areas by association of traditional contributory variables, such as slope and forest cover with variables particularly related to snow cover influence on topography. We integrate a scale dependent roughness parameter accounting for varying winter topography and snow deposition patterns with increasing snow depth. To this aim, roughness was calculated and modeled using elevation models of the winter and summer terrain derived from high-resolution measurements performed by terrestrial LIDAR and airborne LIDAR.

This approach allows for example to define different release area scenarios depending on snow depth. In the future, we hope that such tools, together with avalanche dynamics models, help to improve hazard mitigation strategies not only for extreme avalanches, but also for smaller avalanches affecting roads or ski resorts.

P13

The «Monitor to measure the integral transmittance of windows» (MITRA)

Walter Benjamin¹, Fehlmann André², Finsterle Wolfgang¹, Schmutz Werner¹

¹ Physikalisches-Meteorologisches Observatorium Davos/World Radiation Center, Davos, Switzerland

² Institute for Astronomy, University of Hawaii, Pukalani, USA

The Cryogenic Solar Absolut Radiometer (CSAR), designed and built at the National Physics Laboratory (NPL) in London, aims to reduce the uncertainty of terrestrial Direct Solar Irradiance (DSI) measurements from 0.3% to 0.01%. Terrestrial DSI measurements are important to accurately determine the earth's energy budget of incoming and outgoing radiation and are thus indispensable for investigations of the earth's climate system. Because the window of a cryogenic radiometer has a spectrally dependent reflectivity and absorptivity, the integral transmittance of the broad-band solar irradiance needs to be determined in parallel to correct the power reading of the CSAR instrument. Therefore, the MITRA instrument aims to measure the integral transmittance of the CSAR window with an uncertainty of less than 0.01%. We report on the progress that was made to reduce the uncertainty of the MITRA.

The MITRA instrument has two radiation absorbing cavities, both resulting in a temperature rise against a common heat sink under irradiated conditions. One of the two cavities is periodically covered by a window from the same production batch as the one used for the CSAR instrument. The ratio of the two detectors' temperature rise is used to calculate the integral transmittance t_{int} of the window.

Recent instrument design improvements include the electrical separation and shielding of the motor driving the window guiding rail and the implementation of high accuracy current and voltage measurement devices. These design improvements show an increase in the average accuracy from 0.04% down to less than 0.003% ($k=1$) for a non-irradiated dark case. This proves that the temperature sensing and readout electronics perform well and meet the intended accuracy goal of 0.01%. First measurements of the integral transmittance of a quartz window under laboratory conditions show that the improved instrument allow now for detecting diurnal variations of t_{int} with an accuracy of 0.014%.

P14

Vernetzungskonzepte für Smart Home Anwendungen mittels kostengünstiger Plattformlösungen und bestehender Standards

Zgaga, Janez^{1,2}

¹ Fakultät für Naturwissenschaft und Technik, Freie Universität Bozen, Bozen, Italien

² Innovation Engineering Center, Fraunhofer Italia Research, Bozen, Italien

Seit Jahren ist in mehreren Bereichen des täglichen Lebens ein Trend hin zu immer stärker vernetzten Geräten erkennbar¹. Dieser Trend hält nach wie vor an und entwickelt sich stetig weiter. Der Trendbegriff dazu lautet «Internet of Things», zu Deutsch «Internet der Dinge»: die steigende Kommunikationsfähigkeit von elektronischen Geräten und deren direkte Anbindung an das Internet².

Ein Bereich der diesbezüglich trotz seiner Bedeutung bisher ein Schattendasein geführt hat, rückt nun immer mehr in den Mittelpunkt: eines der sinnvollsten Anwendungsgebiete der Gerätevernetzung ist der Gebäudebereich, in diesem Zusammenhang «Smart Home» genannt³. Mehrere Studien zeigen diesbezüglich das wirtschaftliche und technische Entwicklungspotential in diesem Bereich⁴. Grösste Potentiale und Schwierigkeiten lassen sich dabei im Rahmen des Energiemanagements («Smart Metering») und im Bereich des unterstützen Wohnens («Ambient Assistent Living») identifizieren⁵. Trotz des unter Endverbrauchern sehr bekannten Themas und deren positiver Grundhaltung zum Thema Smart Home, sind die größten Hemmnisse die hohen Kosten und die mangelnden einheitlichen Standards⁶. Der im Vergleich zu elektronischen Geräten viel längere Lebenszyklus eines Ge-

bäudes, fordert langlebige, zuverlässige Lösungen; eine Anforderung die angesichts der vielen bestehenden Insellösungen (Z-Wave, Zigbee, digitalSTROM, KNX,...) nicht erfüllt wird.

In diesem Beitrag werden Konzepte vorgestellt, die anhand von offenen Plattformen und bekannten, etablierten Kommunikationsstandards eine langlebige und nachhaltige Interoperabilität von vernetzten Geräten ermöglichen. Dabei werden die Möglichkeiten von kostengünstigen, nicht proprietären Elektroniklösungen (Arduino, Raspberry Pi) mit bestehenden Vernetzungskonzepten (TCP/IP, WLAN, Ethernet, Powerline Communication) verknüpft, mit dem Ziel, die Machbarkeit und die Potentiale einer erschwinglichen und zukunftsfähigen Heimvernetzung aufzuzeigen.

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P15

Non-invasive biomechanical monitoring of bone healing in a dynamized bone defect in sheep

Eberli Ursula, Ernst Manuela, Schwyn Ronald, Stadelmann Vincent, Windolf Markus
Biomedical Services, AO Research Institute, Davos, Switzerland

Nowadays clinicians do not have a quantitative tool to evaluate the stability of healing bone. Computed tomography (CT) provides structural information about calcified tissues. However, in presence of fixation devices the occurrence of metallic artefacts limits the image quality. We developed a radiolucent implant with an in-built displacement sensor to monitor bone healing of a small defect in the sheep tibia both visually and mechanically. Since several studies have shown that mechanical stimulation influences bone healing¹, the implant was designed to be axially dynamizable in compression. The implant's metallic ends were connected by two carbon rods providing radiolucency and allowing sliding capacity. Our aim was to assess and evaluate temporal patterns of bone healing in a dynamized bone defect in two adult Swiss white alpine sheep during 7 months.

At surgery, the implant was fixed medially on the left tibia and a 6 mm defect was created using an oscillating saw. Thirteen CT scans were acquired during the healing period at a resolution of 0.63 mm. A phantom was used to convert CT units into bone density values. Regions of interest were defined in the post-op scans and scan data of the following time points were registered to it. Interfragmentary motion was monitored continuously with on-board data processing over the first four months.

The two sheep showed very different defect healing, with one specimen forming proper callus and showing bone densification; but the other showing no visible callus formation and poor bone densification. Data analysis of the displacement sensor is still on going.

The difference may originate from several factors such as diverse anatomical constitutions, variable sliding capacity of the implants and so forth (work in progress). So far, our custom radiolucent implant allows the acquisition of perfect CT images without any artefacts and has proven to be mechanically reliable.

Reference: ¹ Hente R, Fuchtmeyer B, Schlegel U, et al. The influence of cyclic compression and distraction on the healing of experimental tibial fractures. *J Orthop Res.* 2004 22(4): 709–715.

P16

Improving the quality of surgical cartilage repair

Gardner Oliver^{1,2}, Alini Mauro¹, Archer Charles³, Musumeci Giuseppe⁴, Stoddart Martin¹

¹ Musculoskeletal Regeneration, AO Research Institute, Davos, Switzerland

² Cardiff Institute of Tissue Engineering and Repair, University of Cardiff, Cardiff, Wales

³ College of Medicine, University of Swansea, Swansea, Wales

⁴ Department of Biomedical Science, University of Catania, Catania, Italy

Introduction: Articular cartilage is found within joints such as the knee and the elbow, its role is to provide a smooth shock-absorbing surface to allow free and easy movement of the joint. Unlike other tissues of the body, cartilage does not have a natural repair response; this means that when damage does occur the cartilage remains unrepaired, leading to deterioration in cartilage function and eventually osteoarthritis.

A range of surgical techniques are available to repair areas of damage and prevent progressive deterioration. One of the most successful of these techniques, known as articular chondrocyte transplantation (ACI), involves the collection of cartilage cells from the damaged joint and their reimplantation within tissue engineering constructs to encourage repair of the damaged area. This project looked at the potential for improving the quality of repair material by changing the location of cells within these scaffolds.

Methods: Our group has previously developed a device that mimics the mechanical environment joint and shown that this provides a chondrogenic stimulus to human cells in constructs similar to those used for cartilage repair. In this work a small proportion (10%) of the total number of cells within the constructs were moved to the loaded surface of the scaffolds in an attempt to increase the amount of cartilage-like matrix produced in response to this form of mechanical load.

Results: The results of biochemical, histological and gene expression analysis show that moving 10% of the total number of cells to the loaded surface of the construct lead to an improvement in the deposition of cartilage-like material in response to mechanical load.

Discussion: This project has demonstrated that the repair tissue generated using techniques like ACI could be improved through changes in the location of a small proportion of the cells used to the loaded surface of the scaffold.

P17

Are serious games promoting mobility an attractive alternative to conventional self-training for elderly people?

Hasselmann Viviane¹, Bachmann Stefan², Oesch Peter¹

¹ Physiotherapy Department, Kliniken Valens, Walenstadtberg, Switzerland

² Department of Rheumatology and Rehabilitation, Kliniken Valens, Walenstadtberg and Valens, Switzerland

Background: Switzerland experiences a demographic trend towards an ageing population. Maintaining mobility of elderly persons has become a primary goal within healthcare services. Specific inpatient rehabilitation programs increase physical abilities of elderly and reduce institutional placement and mortality (Bachmann, 2010). In older community-dwelling adults, exercise programs significantly reduce the risk of death and falling (Thomas, 2010). Long-lasting and high-intensive multicomponent exercises are most effective (Daniels, 2008). Those exercise programs are conventionally instructed by physiotherapists using written exercise descriptions thereby allowing self-exercising. However, the compliance of elderly people to execute self-exercise programs varies considerably. These programs are often considered as tedious and boring, and so prematurely stopped (Phillips, 2004). An alternative to increase patient's motivation for self-exercising is using serious games promoting mobility.

Objective: The aim of this study is to determine whether elderly people in rehabilitation setting show higher adherence to exercise programs when using serious games than when performing

conventional exercises. Secondly, we explore to which extent balance abilities vary according to the mode of exercising.

Methods: Participants are randomly allocated to conventional exercise programs or to serious games with Xbox Kinect® and FitBit®. Self-exercise programs are performed during the inpatient rehabilitation stay. All participants are entitled to two additional time-slots (2 x 30 min/day) for 10 days specifically for self-exercising. Primary outcome is intensity of exercises performed, extracted from a log book. Secondary outcomes are balance abilities measured by the Berg Balance Score and fear of falling measured by the Fall Efficacy Scale.

Discussion: To our knowledge, this study is the first to compare conventional self-training programs with serious games among elderly persons. Results of this study will provide insight into the effectiveness of serious games promoting mobility and contribute to our understanding of the motivational potential of serious games in elderly people.

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P18

Kortikale Dicke und Porosität am proximalen Humerus korrelieren mit dem osteoporotischen Knochensubstanzverlust: Eine Analyse der mikrostrukturellen Umbauprozesse

Helfen Tobias^{1,2}, Eberli Ursula¹, Gueorguiev Boyko¹, Müller Peter E.³, Richards R. Geoff¹, Schmidutz Florian³, Sprecher Christoph M.¹

¹ AO Research Institute, Davos, Schweiz

² Chirurgische Klinik, Universität München (LMU), München, Deutschland

³ Universität München (LMU), Orthopädische Klinik, München, Deutschland

Fragestellung: Proximale Humerusfrakturen stehen in direktem Zusammenhang zum Knochensubstanzverlust im höheren Lebensalter. Studien am Radius und der Tibia zeigen, dass neben dem trabekulären Knochensubstanzverlust auch den mikrostrukturellen Umbauprozessen an der Kortikalis eine entscheidende Rolle zukommt. Für den Humerus liegen trotz seiner Frakturhäufigkeit im Alter hierrüber kaum Daten vor und wurden daher analysiert.

Methodik: 26 Humeri [68±23 Jahren (Mittel±SD), 19–90 Jahren (Intervall)] wurden mittels HR-pQCT (XtremeCT, Scanco) (Auflösung 82 µm) gescannt. Die Proben wurden anhand der Knochendichte (Bone-mineral-density [BMD]) (145±47 mgHA/cm³, 69–254 mgHA/cm³) in eine Gruppe mit guter (n=13) und schlechter (n=13) Knochenqualität eingeteilt.

Der proximale Humerus wurde semi-automatisch in den spongiösen und kortikalen Anteil unterteilt. Es folgte eine Analyse der kortikalen Dicke [Cortical Thickness [Ct.Th]] und der kortikalen Porosität [Cortical Porosity [Ct.Po]] für das Collum chirurgicum und den Schaft. Der Einfluss des BMDs auf die Ct.Th, die Ct.Po und das Alter wurde mittels R² Pearson's coefficient evaluiert. Der Vergleich der Gruppen erfolgte mittels ungepaartem t-test (p≤0.05 signifikant). Zusätzlich wurden repräsentative Humerusproben mittels hochauflösenden Kontaktradiographien und histologischen Schnitten evaluiert.

Ergebnisse und Schlussfolgerung: Am Collum chirurgicum betrug die mittlere Ct.Th 1.30±0.37 mm. In der Gruppe mit guter BMD betrug diese 1.48±0.37 mm und bei schlechter BMD 1.11±0.27 mm, was einer signifikanten Reduktion um 34% (p<0.01) entspricht. Die mittlere Ct.Po betrug 26±10%; mit 20±8% bei guter BMD und 31±9% bei schlechter BMD, was einem Anstieg von 55% (p<0.01) entspricht.

Am Schaft betrug die mittlere Ct.Th 2.46±0.83 mm, mit 2.97±0.63 mm bei guter BMD und 1.96±0.69 mm bei schlechter BMD, was einer signifikanten Reduktion um 34% (p<0.01) entspricht. Die mittlere Ct.Po betrug 10±6%; 7±3% bei guter BMD und 14±6% bei schlechter BMD, was einem Anstieg von 130% (p<0.01) entspricht. Diese mikrostrukturellen Umbauprozesse mit einer deutlichen Reduktion der Ct.Th und einem Anstieg der Ct.Po zeigten sich ebenfalls in den hochauflösenden Kontaktradiographien und histologischen Schnitten.

Die BMD war ein guter Prädiktor für die Ct.Th. (R²=0.50, p<0.01) und Ct.Po (R²=0.46, p<0.01) am Schaft. Der BMD korrelierte mässig am Hals für die Ct.Th (R²=0.25, p<0.01) und Ct.Po (R²=0.25, p<0.01). Das Alter korrelierte ebenfalls mässig mit dem BMD (R²=0.31, p<0.01). Zusammenfassend zeigt sich, dass der osteoporotische Knochensubstanzverlust auch am proximalen Humerus zu einer erheblichen Verminderung der kortikalen Dicke und einem deutlichen Anstieg der kortikalen Porosität führt. Da die Kortikalis am Collum chirurgicum wesentlich zur Stabilität beiträgt, dürften die mikrostrukturellen Umbauprozesse einen erheblichen Einfluss auf das Auftreten von altersbedingten proximalen Humerusfrakturen haben und sollten bei künftigen Untersuchungen vermehrt berücksichtigt werden.

P19

Quantitative measurements of antigen-specific immunoglobulins using an evanescent biosensor

Huitema Carly, Akdis Cezmi A., Cramer Reto, Rhyner Claudio, Schawaller Manfred

Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

The quantification of IgE is important for the diagnosis and understanding of allergic disease, for example, identification of antigen specific IgE can assist in diagnosing human allergy. Research of asthma and allergy is frequently done using mouse models, and quantifying the amount of antigen specific antibodies is an important parameter of experiments.

The model antigen used in mouse models is ovalbumin (OVA), and to quantify OVA-specific antibodies in serum we used an evanescent instrument in combination with a disposable evanescent polystyrene biosensor chip containing eight wells for samples. With the evanescent instrument, there is illumination only in the bottom ~200nm of a well due to the way the laser light beam is directed by the geometry of the biosensor chip. With specific biomolecular coatings of the wells, samples of interest with fluorescently labeled detectors can accumulate in the evanescent field when binding to the well bottom, and emitted photons can be detected in real-time. The binding rate is both diffusion limited and concentration dependent. Quantitative results can be achieved within ten minutes requiring no extra manipulation steps such as incubation and washing.

To measure OVA-specific antibodies in mouse serums, we developed two different assay formats. To quantify OVA-specific mouse IgE, we coated the biosensor chip wells with anti-mouse IgE and detected with a fluorescently labeled OVA molecule. We could also measure OVA-specific immunoglobulins in a double antigen sandwich assay (DAS) where we coated the biosensor wells with OVA and detected with fluorescently labeled OVA. In this second assay, it was remarkable that we were able to use the DAS one-step ten minute assay format as there were no wash steps following sample addition. This opens the possibility of adopting the DAS method for antibody screening in the diagnosis of numerous diseases (i.e. HIV, Hepatitis B, Tuberculosis).

P20

Medial bony support as an indicator for the selection of the osteosynthesis procedure in complex bicondylar proximal tibia fractures

Johannson Bettina, Sommer Christoph, Stillhard Philipp
Departement Chirurgie, Kantonsspital Graubünden, Chur, Switzerland

Objectives: Various methods for the fixation of complex bicondylar proximal tibia fractures (AO 41-C-type) are published. Lateral locking plate fixation and medial-lateral double plate fixation are based on different biomechanical concepts. Our hypothesis was that lateral locking plate fixation using a strong angular stable implant yields similar results compared to double plate fixation even in cases with missing medial bony buttress.

Methods: We performed a retrospective radiological analysis of a comparable group of patients treated either with a single less invasive lateral proximal stabilization system (LISS-PLT) or medio-lateral double LCP fixation. Included were local resident patients with complete radiological follow-up until fracture consolidation. The main outcome parameter was the measurement of the medial proximal tibia angle (MPTA) postoperatively and after fracture healing.

Results: From 2002 until 2012, 137 proximal tibia C-type fractures were treated at our institution. 60 patients (30 patients in both groups) were locally resident and could be evaluated. Patient's characteristics were similar in sex, age, fracture classification and concomitant soft tissue injuries. In the LISS group, 18 showed no medial bony buttress. 13 of these showed an increased variation between two and five degrees, whereas only 1 out of 12 patients with medial bony buttress revealed variation.

A total of 14/30 patients in the LISS group showed an increased variation compared to 0/30 patient in the LCP group.

Conclusion: A unilateral LISS fixation of complex proximal tibia fractures showed to be sufficient in fractures with bony medial support. Due to an increase in variation, double plate osteosynthesis should be preferred in fractures lacking medial bony buttress.

P21

Measurements of allergen specific antibodies during allergen specific immunotherapy using the evanescent field method: A comparison

Olzhausen Judith¹, Akdis Cezmi¹, Cramer Reto¹, Jutel Marek², Rhyner Claudio¹, Schawaller Manfred¹

¹ Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

² Department of Clinical Immunology, Wrocław Medical University, Wrocław, Poland

Currently, allergen specific immunotherapy (SIT) represents the only curative treatment approach for allergic diseases. Increasing doses of an allergen are applied to an allergic patient with the aim to induce peripheral T-cell tolerance and a shift from a TH2 to a TH1/Treg-biased immune response. The aim of this study is the development of diagnostic assays for the monitoring of changes in levels of allergen-specific antibodies during SIT using the evanescent field technology.

The EVA-biosensor is a near patient testing device that allows fast and quantitative measurements of minute amounts of biomolecules with reduced wash and incubation steps, compared with standard ELISA methods.

In an EVA-Assay, the major allergen responsible for cat allergy, Fel d1, was immobilized on the surface of a polystyrene EVA-biosensor chip. The detection of Fel d1 specific IgE in human serum was achieved by a human anti IgE antibody labeled with fluorescent Allophycocyanine (APC). The detection limit of this assay is 0.17 kUA/L Fel d1 specific IgE and as sensitive as an ELISA (LOD=0.14 kUA/L) which was performed with the same components. Serums from allergic patients were measured by EVA, ELISA, and ImmunoCapTM and the results obtained with the three detection systems showed significant correlations.

In a second example of SIT, serum samples from 8 different Mugwort pollen allergic patients undergoing SIT were also measured

in a direct assay, using the major allergen Art v1. APC labeled anti human IgE or anti human IgG4 served as detection antibodies. During the first months of SIT an increase and in a later stage a decrease of Art v1 specific IgE were observed. The levels of Art v1 specific IgG4 starts to increase after the first month of SIT. These data results in a decrease of the Art v1 specific IgE/IgG4 ratio, commonly accepted as one indicator of successful SIT.

P22

Bilocal recurrence of a neuroendocrine carcinoma of the small intestine, a case report

Peiffer Simon¹, Cathomas Richard², Villiger Peter¹

¹ Department for visceral surgery, Kantonsspital Graubünden, Chur, Switzerland

² Department for oncology, Kantonsspital Graubünden, Chur, Switzerland

Introduction: With an incidence of 0,29/100.000 the malignant forms of neuroendocrine tumors (NET) of the small intestine represent a very rare disease. Recurrence rate of completely resected NET of the small intestine has not clearly been described yet, but depends on the proliferation rate (Ki-67). We report a recurrence in a 64-year-old female with NET of the proximal ileum after 4 years.

Case report: A 64-year-old female with family history for colorectal and gastric carcinoma underwent regular screening by her GP. Because of asymptomatic elevation of CA 19-9 a CT-scan was carried out and revealed a tumor of the small intestine of 14 mm in diameter. The tumor was resected and histological workup classified it as a neuroendocrine tumor (pT4, N1, G1, Ki-67 < 1%). After 4 years of follow-up, CT-scan showed two suspicious lesions of the small intestine. Gallium DOTATOC-PET-CT verified tumor recurrence in both sites and segmental resection of the small intestine was performed again. Histological exam of the tumor showed the same histology of NET as before (pT2, N1, G1, Ki-67 < 1%).

Discussion: Bilocal recurrence of NET of the small intestine with high differentiation and low proliferation rate is rather unlikely with no exact data for recurrence rate in current literature. Following the latest ENETS guidelines of 2009 follow-up should be carried out with regular CT-scan and measurement of chromogranin A according to TNM stage and Ki67 rate at diagnosis. For exact diagnosis and localization somatostatin receptor imaging, either as octreotide scintigraphy or Gallium DOTATOC-PET-CT, should be used. As DOTATOC-PET may have higher sensitivity than octreotide scintigraphy, according to latest results it should nowadays be favored. Therefore, the two new detected tumors in 2013 could just have been missed by octreotide scintigraphy in 2009.

Conclusion: Even in case of low proliferation index, follow-up for NET should be performed according to current guidelines in order not to miss rare but possible tumor recurrence. In case of changing diagnostic matters, reduced comparability has to be taken in concern.

P23

Der zementfreie Oberflächenersatz der Schulter induziert ein knöchernes Stress-Shielding: Eine humane Explantate- und Finite-Elemente-Analyse

Sprecher Christoph M.¹, Agarwal Yash¹, Gueorguiev Boyko¹, Müller Peter E.², Richards R. Geoff¹, Schmidutz Florian^{1,2}

¹ AO Research Institute, Davos, Schweiz

² Orthopädische Klinik, Universität München (LMU), München, Deutschland

Fragestellung: Der zementfreie Oberflächenersatz der Schulter (CSRA) dient der anatomischen Gelenksrekonstruktion mit nur minimalem Knochensubstanzverlust. Aufgrund der röntgendichten Implantate liegen jedoch nur wenige Daten über die knöchernen Integration und die unter dem Implantat entstehenden Knochenumbauprozesse vor, weshalb diese untersucht wurden.

Methodik: Die Lastübertragung und das Stress-Shielding von zwei unterschiedlichen CSRA Designs, Epoca RH (kronenförmige Stem-Fixierung) und Copeland (zapfenförmige Stem-Fixierung)

wurden anhand einer 3-dimensionalen Finite-Elemente-Analyse (FEA) evaluiert. Hierzu wurden die Implantate virtuell in jeweils einem normalen und osteoporotischen Knochen implantiert und dabei die Veränderungen der Lastübertragung in 8 Regionen unter dem Implantat bestimmt. Anschliessend wurden die in der FEA virtuell ermittelten Knochenumbauprozesse mit den Ergebnissen von humanen CSRA Explantaten (n=8) und nativen Humerusköpfen anhand von Kontaktradiographien aus dem Implantat- und Kopffzentrum verglichen.

Ergebnisse und Schlussfolgerung: Die FEA zeigte für beide CSRA Designs eine vermehrte Kraffteinleitung im Bereich der Stems und am äusseren Implantaterand, was auf eine erhöhte Knochenapposition in diesen Bereichen hinweist. Hingegen wurde eine deutliche Reduktion der Kraffteinleitung (Epoca 50–85% und Copeland 31–93%) für die zentralen Knochenlagerregionen direkt unter dem Implantat ermittelt, was auf einen deutlichen Knochenabbau hinweist.

Relativ hohe und inhomogene Stressspitzen wurden insbesondere im osteoporotischen Knochenmodell sowie am distalen Stem der Copeland Prothese beobachtet.

Die Analyse der humanen CSRA bestätigte die FE Analysen. Die Explantate wiesen vermehrt Knochensubstanz im Bereich der Stems und dem äusseren Implantaterand auf, wohingegen sich eine deutlich reduzierte Knochensubstanz im Bereich des zentralen Implantatelagers fand.

Zusammenfassend weisen beide CSRA Designs klare Stress-Shielding Zeichen in der FEA und den humanen Explantaten auf. Das Stress-Shielding führt zu einer Lastübertragung an den Stems sowie dem Implantaterand und führt zu einem Abbau des zentralen Knochenlagers. Ob und wie sich diese knöchernen Umbauprozesse auf die klinischen Ergebnisse und Standzeiten auswirken ist unklar und bedarf weiterer Untersuchungen.

P24

Characteristics of human primary osteoblasts from osteoarthritic femoral heads

Stanciuc Ana-Maria, Alini Mauro, Peroglio Marianna, Stoddart Martin

Musculoskeletal Regeneration, AO Research Institute, Davos, Switzerland

Introduction: Osteoarthritis is a worldwide problem affecting currently over 40 million Europeans that dramatically lowers the quality of life. Painkillers and anti-inflammatory drugs are generally used for the treatment until surgery is required. Total hip or knee replacement is the standard, whereby ceramic implants have the advantage of low debris formation and therefore reduced risk of osteolysis. The response to an implant is determined by two major components: implant design and bone characteristics. Here, we report about characterization of bone tissue obtained from human osteoarthritic femoral heads.

Methods: Human primary osteoblasts were isolated from osteoarthritic femoral heads obtained from patients undergoing hip replacement (approved by Ethic Commission Graubünden 18/02). Osteoblasts were obtained by cell outgrowth from bone chips¹. The cells were expanded in vitro and frozen at passage². The proliferation rate was monitored during expansion. After thawing and expansion, cells were seeded on tissue culture plastic and cultured in osteogenic conditions for 21 days. Cell growth was monitored by DNA quantification and mineralization was evaluated by alkaline phosphatase activity and alizarin red staining at regular time points. The expression of relevant genes (osteocalcin, bone sialoprotein and the transcription factor runx2) was also assessed.

Results and discussion: The growth rate of osteoblasts decreased with repeated outgrowth from the bone chips, suggesting that later osteoblasts might be at a more differentiated stage. Similar to previous studies, we have observed high donor variability. However, we could observe a trend for lower cell yield with older donors. No correlation was found between cell growth rate and age. Further analyses on the osteogenic potential of these cells are underway.

Conclusions: We observed lower cell yield, but not cell growth rate, with age and further analyses will focus on the osteogenic potential of these cells. Cell proliferation strategies may be of benefit for elderly patients.

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P25

Isolation and characterization of IL-22 producing T cells

Wawrzyniak Marcin¹, Akdis Cezmi¹, Akdis Mübecel¹, Breedveld Annelot^{1,2}, Rebane Ana¹, Rhyner Claudio¹, Rückert Beate¹, Wawrzyniak Paulina¹

¹ Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

² Cell Biology and Immunology Group, Wageningen University and Research Centre, Wageningen, Netherlands

IL-22 is mainly produced by T helper cells (Th17, Th22) and at lower levels by $\gamma\delta$ T, NKT and LT α cells. IL-22 binds to IL-22R composed of the IL-22R1 and IL-10R2 subunits. It is thought that IL-22 is a bi-functional cytokine depending on cytokine environment. The only obstacle to study IL-22 biology is lack of an assay, which allows sorting alive IL-22-producing cells, and IL-22-producing cells that can co-produce IL-17 and/or INF- γ . The aim of our study is the characterization of IL-22 producing cells from blood, tonsils and sinus, and to compare single IL-22-producing cells with IL-17, IFN- γ and IL-22 co-producing cells to determinate the role of other cytokines in the functions of IL-22.

We developed IL-22 secretion assay, which allows detection and sorting of alive IL-22-producing cells. To find optimal IL-22 inducing conditions, we used intracellular staining of cytokines, magnet-activated cell sorting, flow cytometry and IL-22 ELISA.

For the first time, we show that T cells sorted with IL-22 secretion assay show higher IL-22 mRNA and protein levels as compared to IL-22 negative cells. IL-22 secretion assay allows to sort IL-22 producing cells and to perform co-culture experiments with epithelial cells. We analyzed IL-22 production and Th1/Th2/Th17 cytokines co-production by T cells isolated from blood, palatine tonsils, and sinus. Moreover, for the first time we show that differentiated Th2 cells are able to produce IL-22 together with IL-4 and IL-13, which may suggest potential role of IL-22 in allergic diseases.

In summary, isolation and characterization of IL-22 producing cells by IL-22 secretion assay from different biological materials allows us to better understand their frequency, functional properties and role in tissue biology.

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