Scientific Highlights

SHORT OVERVIEWS ON RECENTLY PUBLISHED SCIENTIFIC EVIDENCE.

Issue 3/2021

Edited by Dr Pooja Nair

in this issue

EDITOR'S CHOICE

A novel fully tapered, self-cutting tissue-level implant: non-inferiority study in minipigs
(E El Chaar et al. 2021)

and

Clinical performance of narrow-diameter titanium-zirconium implants in immediately loaded fixed full-arch prostheses: a 2-year clinical study
(F M Coskunses et al. 2021)

Long term clinical performance of 10 871 dental implants with up to 22 years of follow-up: A cohort study in 4247 patients
(D French et al. 2021)

Greater Osseointegration Potential with Nanostructured Surfaces on TiZr: Accelerated vs. Real-Time Ageing
(A Stavropoulos et al. 2021)

Editor's choice

Clin Oral Investig. 2021 Apr 16. doi: 10.1007/s00784-021-03912-w.

A novel fully tapered, self-cutting tissue-level implant: non-inferiority study in minipigs

E El Chaar, A Puisys, I Sabbag, B Bellón, A Georgantza, W Kye, B E Pippenger

FREE FULL TEXT

Study objectives and methods

To assess the osseointegration and crestal bone level maintenance of a novel fully tapered self-cutting tissue-level implant for immediate placement (test) compared to a clinically established tissue-level implant (control) in moderate bone quality. Test and control implants were compared in 3 groups, i.e., small-, medium-, and large-diameter implants in an edentulous mandibular minipig model with moderate bone quality after 12 weeks of healing. Histometrically derived bone-to-implant contact (BIC) and first bone-to-implant contact (fBIC) were subjected to statistical non-inferiority testing. Maximum insertion torque values in artificial bone were assessed for comparison.

Results

- BIC values for the tests and control implants for all 3 diameters were comparable and non-inferior: small diameter (61.30 ± 10.63% vs. 54.46 ± 18.31%) (p=0.99), medium diameter (60.91 ± 14.42 vs. 54.68 ± 9.16) (p=0.55), and large diameter (45.60 ± 14.67 vs. 52.52 ± 14.76) (p=0.31).
- fBIC values for test implants were higher and non-inferior compared to control implants in all three groups. Test implants further showed distinctly higher maximum insertion torque values compared to control implants.

Conclusions

- The investigated novel tissue-level implant is able to achieve high levels of primary and secondary implant stability under simultaneous preservation of crestal bone levels. This qualifies the studied implant as an attractive candidate for immediate placement in bone of limited quality.

*Adapted from E El Chaar et al., Clin Oral Investig. 2021 Apr 16., for more info about this publication click **HERE***

Int J Implant Dent. 2021 Apr 16; 7(1):30. doi: 10.1186/s40729-021-00312-3.

Clinical performance of narrow-diameter titanium-zirconium implants in immediately loaded fixed full-arch prostheses: a 2-year clinical study

F M Coskunses and Ö Tak

Study objectives and methods

FREE FULL TEXT

The aim of this study was to evaluate the outcomes of immediate fixed full-arch prostheses supported by axial or tilted narrow-diameter Ti-Zr implants (3.3 mm) (Roxolid®, Institut Straumann® AG, Basel, Switzerland) (NDIs) in combination with standard-diameter implants up to 2 years' follow-up.
The study was conducted at Kocaeli University Faculty of Dentistry from 2016 to 2018. 37 jaws of 28 patients with an average age of 52 years were rehabilitated with fixed full-arch prostheses supported by 179 implants. Cumulative survival rate (CSR), implant success, marginal bone loss (MBL), and prosthetic survival rate as well as complications were analyzed.

Results

- Total CSR of 99.4% and 98.5% for all and narrow implants respectively have been observed at 2 years' follow-up. No prosthesis failures were observed, yielding a cumulative prosthetic survival rate of 100%.
- The NDIs achieved 0.63 mm MBL at 1 year and 1.02 mm at 2 years. The mean MBL at 1 year was 0.51 mm (mandible 0.63 mm/maxilla 0.41 mm) and 0.73 mm (mandible 0.90 mm/maxilla 0.43 mm) at 2 years.
- Both implant angulation and loading protocol did not influence the MBL.

Conclusions

The combination of narrow-diameter implants with standard-diameter implants in immediate fixed full-arch rehabilitation has a good prognosis to become a new standard of care for severely atrophic jaws.
The use of narrow-diameter implants in fixed full-arch rehabilitations in atrophic ridges would be a successful and predictable treatment approach

*Adapted from F M Coskunses et al., Int J Implant Dent. 2021 Apr 16, for more info about this publication click **HERE***

Clin Implant Dent Relat Res. 2021 Mar 25. doi: 10.1111/cid.12994

Long term clinical performance of 10 871 dental implants with up to 22 years of follow-up: A cohort study in 4247 patients

D French, R Ofec, L Levin

FREE FULL TEXT

Study objectives and methods

The present retrospective study was aimed to assess the long-term clinical performance of dental implants in a cohort study of 4247 patients.

A longitudinal observational cohort study was done on all implants performed by a single periodontist from July 1995 to April 2019. The main outcome variables of this study were implant failure and marginal bone level around implants

Results

- The study participants received a total of 10 871 implants with a mean of 2.56 implants per patient. The cohort was followed-up to 22.2 years (mean = 4.5 ± 4.2).
- Among the 4247 patients of the current study, 140 patients (3.3%) experienced a combined total of 178 implant failures.
- According to life table analysis, at the implant level the cumulative survival rate at 3, 5, 10, and 15 years was 98.9%, 98.5%, 96.8%, and 94.0%, respectively while at patient level was 97.4%, 96.7%, 92.5%, and 86% at 3, 5, 10, and 15 years.
- Patients with multiple units were at a greater risk for having an implant failure.
- Baseline bone level was 0.09 ± 0.28 mm while at 8-10 years the mean bone level was 0.49 ± 0.74 mm. The incidence of peri-implant mucositis at the implant level was 9.4% at 2-3 years, 9.3% at 4-5 years, 12.1% at 6-7 years, and 11.9% at 8-10 years.
- The incidence of peri-implantitis was 2%, 2.6%, 3.2%, and 7.1% at 2-3, 4-5, 6-7, and 8-10 years, respectively.
- Cigarette smoking and diabetes mellitus were positively correlated with implant failure.

Conclusions

Though the results are promising and encouraging in terms of survival and bone level over time, it is important to emphasize the potential risk factors and consider them prior to dental implant placement.

*Adapted from D French et al., Clin Implant Dent Relat Res. 2021 Mar 25, for more info about this publication click **HERE***

Materials (Basel). 2021 Mar 29;14(7):1678. doi: 10.3390/ma14071678

Greater Osseointegration Potential with Nanostructured Surfaces on TiZr: Accelerated vs. Real-Time Ageing

A Stavropoulos, R Sandgren, B Bellon, A Sculean, B E Pippenger

FREE FULL TEXT

Study objectives and methods

Surface chemistry and nanotopography of dental implants can have a substantial impact on osseointegration. The aim of this investigation was to evaluate the effects of surface chemistry and nanotopography on the osseointegration of titanium-zirconium (TiZr; Roxolid®) discs, using a biomechanical pull-out model in rabbits.

Two discs each were placed in both the right and left tibiae of 16 rabbits. Five groups of sandblasted acid etched (SLA) discs were tested: (1) hydrophobic without nanostructures (dry/micro) (n = 13); (2) hydrophobic with nanostructures, accelerated aged (dry/nano/AA) (n = 12); (3) hydrophilic without nanostructures (wet/micro) (n = 13); (4) hydrophilic with nanostructures, accelerated aged (wet/nano/AA; SLActive®) (n = 13); (5) hydrophilic with nanostructures, real-time aged (wet/nano/RTA).
The animals were sacrificed after four weeks and the biomechanical pull-out force required to remove the discs was evaluated.

Results

- Adjusted mean pull-out force was greatest for group wet/nano/RTA (64.5 ± 17.7 N) and lowest for group dry/micro (33.8 ± 10.7 N).
- Multivariate mixed model analysis showed that the pull-out force was significantly greater for all other disc types compared to the dry/micro group.
- Surface chemistry and topography both had a significant effect on pull-out force ($p < 0.0001$ for both), but the effect of the interaction between chemistry and topography was not significant ($p = 0.1056$).

Conclusions

The introduction of nanostructures on the TiZr surface significantly increases osseointegration. The introduction of hydrophilicity to the TiZr implant surface significantly increases the capacity for osseointegration, irrespective of the presence or absence of nanotopography.

Adapted from A Stavropoulos et al., Materials (Basel). 2021 Mar 29;14(7):1678, for more info about this publication click HERE

Clin Oral Implants Res. 2021 Apr; 32(4):487-497. doi: 10.1111/clr.13717.

Surface characteristics on commercial dental implants differentially activate macrophages in vitro and in vivo

J O Abaricia, A H Shah, M N Ruzga, R Olivares-Navarrete

Study objectives and methods

Biomaterial implantation provokes an inflammatory response that controls integrative fate. M2 macrophages regulate the response to implants by resolving the inflammatory phase and recruiting progenitor cells to aid healing. We have previously shown that modified titanium (Ti) disks directly induce M2 macrophage polarization. The aim of this study was to examine macrophage response to commercially available Ti or Ti alloy implants with comparable roughness and varying hydrophilicity.

Eleven commercially available Ti (A-F) or Ti alloy (G-K) dental implants were examined in this study. Surface topography, chemistry, and hydrophilicity were characterized for each implant. To compare the immune response in vitro, human monocyte-derived macrophages were seeded on implants and secreted pro- and anti-inflammatory proteins measured. To evaluate the inflammatory response in vivo, mice were subcutaneously instrumented with clinical implants, and implant adherent macrophage populations were characterized by flow cytometry.

Results

- Macrophages on hydrophobic Implant C produced the highest level of pro-inflammatory proteins in vitro.
- In contrast, hydrophilic Implant E produced the second-highest pro-inflammatory response. Implants F and K, both hydrophilics, produced the highest anti-inflammatory protein secretions.
- Likewise, pro-inflammatory CD80hi macrophages predominated in vivo on implants C and E, and M2 CD206 + macrophages predominated on implants F and K.

Conclusions

These findings show that hydrophilicity alone is insufficient to predict the anti-inflammatory effect on macrophage polarization and that other properties-surface composition or topography-determine immune modulation.

This in vivo model may be a useful screening method to compare the immunomodulatory response to clinical implants of disparate geometry or size.

*Adapted from J O Abaricia et al., Clin Oral Implants Res. 2021 Apr;32(4):487-497, for more info about this publication click **HERE***

Biology (Basel). 2021 Apr 22;10(5):356. doi: 10.3390/biology10050356.

Impact of Implant Surface Material and Microscale Roughness on the Initial Attachment and Proliferation of Primary Human Gingival Fibroblasts

M A Rausch, H Shokoohi-Tabrizi, C Wehner, B E Pippenger, R S Wagner, C Ulm, A Moritz, J Chen, O Andrukhov

FREE FULL TEXT

Study objectives and methods

Due to the rising demand for zirconia (Zr) based implant systems, it is important to understand the impact of Zr and titanium (Ti) implants and particularly their topography on soft tissue healing. As human gingival fibroblasts (hGFs) are the predominant cells in peri-implant soft tissue, we focused on examining the effect of implant material and surface roughness on hGFs' initial attachment, growth and the expression of proteins involved in the focal adhesion.

hGFs isolated from eight healthy donors were cultured on the following surfaces: smooth titanium machined surface (TiM), smooth zirconia machined surface (ZrM), moderately rough titanium surface (SLA), or moderately rough zirconia surface (ZLA) for up to 14 days. The initial attachment of hGFs was evaluated by scanning electron microscopy.

Cell proliferation/viability was assessed by cell counting kit 8. Focal adhesion and cytoskeleton were visualized by a focal adhesion staining kit. The gene expression of focal adhesion kinase (FAK), α-smooth muscle actin (α-SMA), and integrin subunits ITG-β1, ITG-β4, ITG-α4, ITG-α5, ITG-α6, was evaluated by qPCR.

Results

- Cell proliferation/viability was slightly decreased by moderately rough surfaces, whereas no effect of surface material was observed.
- Cell morphology was strikingly different between differently treated surfaces: on machined surfaces, cells had elongated morphology and were attached along the grooves, whereas on moderately rough surfaces, cells were randomly attached.
- Surface roughness had a more pronounced effect on the gene expression compared to the surface material. The expression of FAK, α-SMA, ITG-β4, ITG-α5, and ITG-α6 was enhanced by moderately rough surfaces compared to smooth surfaces.

Conclusions

Within the limitations of this in vitro study, it can be concluded that the behavior of primary hGFs is primarily affected by surface structure, whereas no apparent advantage of Zr over Ti could be observed.

Adapted from M A Rausch et al., Biology (Basel). 2021 Apr 22;10(5):356, for more info about this publication click HERE

Sci Rep. 2021 Apr 14;11(1):8152. doi: 10.1038/s41598-021-87507-1.

A meta-analysis indicating extra-short implants (≤6mm) as an alternative to longer implants (≥8mm) with bone augmentation

X Yu, R Xu, Z Zhang, Y Yang, F Deng

FREE FULL TEXT

Study objectives and methods

Extra-short implants, of which clinical outcomes remain controversial, are becoming a potential option rather than long implants with bone augmentation in atrophic partially or totally edentulous jaws. The aim of this study was to compare the clinical outcomes and complications between extra-short implants (≤ 6 mm) and longer implants (≥ 8 mm), with and without bone augmentation procedures.

Electronic (via PubMed, Web of Science, EMBASE, Cochrane Library) and manual searches were performed for articles published prior to November 2020. Only randomized controlled trials (RCTs) comparing extra-short implants and longer implants in the same study reporting survival rate with an observation period at least 1 year were selected. Data extraction and methodological quality (AMSTAR-2) was assessed by 2 authors independently. A quantitative meta-analysis was performed to compare the survival rate, marginal bone loss (MBL), biological and prosthesis complication rate. Risk of bias was assessed with the Cochrane risk of bias tool 2 and the quality of evidence was determined with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. 21 RCTs were included, among which two were prior registered and 14 adhered to the CONSORT statement.

Results

- No significant difference was found in the survival rate between extra-short and longer implant at 1- and 3-years follow-up (RR: 1.002, CI 0.981 to 1.024, P = 0.856 at 1 year; RR: 0.996, CI 0.968 to 1.025, P = 0.772 at 3 years, moderate quality), while longer implants had significantly higher survival rate than extra-short implants (RR: 0.970, CI 0.944 to 0.997, P < 0.05) at 5 years.
- Interestingly, no significant difference was observed when bone augmentations were performed at 5 years (RR: 0.977, CI 0.945 to 1.010, P = 0.171 for reconstructed bone; RR: 0.955, CI 0.912 to 0.999, P < 0.05 for native bone). Both the MBL (from implant placement) (WMD: - 0.22, CI - 0.277 to - 0.164, P < 0.01, low quality) and biological complications rate (RR: 0.321, CI 0.243 to 0.422, P < 0.01, moderate quality) preferred extra-short implants.
- However, there was no significant difference in terms of MBL (from prosthesis restoration) (WMD: 0.016, CI - 0.036 to 0.068, P = 0.555, moderate quality) or prosthesis complications rate (RR: 1.308, CI 0.893 to 1.915, P = 0.168, moderate quality).

Conclusions

The placement of extra-short implants could be an acceptable alternative to longer implants in atrophic posterior arch. Further high-quality RCTs with a long follow-up period are required to corroborate the present outcomes.

*Adapted from X Yu et al., Sci Rep. 2021 Apr 14;11(1):8152, for more info about this publication click **HERE***

Clin Oral Implants Res. 2021 Mar 13. doi: 10.1111/clr.13742.

Enamel matrix derivative promotes new bone formation in xenograft assisted maxillary anterior ridge preservation-A randomized controlled clinical trial

F Mercado, C Vaquette, S Hamlet, S Ivanovski

Study objectives and methods

To compare the effectiveness of deproteinized bovine bone mineral with 10% collagen alone (DBBMC) or with enamel matrix derivative (DBBMC-EMD) in ridge preservation.

42 maxillary anterior teeth were extracted and received either a DBBMC (control) or DBBMC-EMD (test) treatment protocol. CBCT taken before and 4 months after the extraction procedure was used to measure changes in alveolar ridge width (RW), buccal bone height (BH) and palatal bone height (PH). Bone cores were harvested during implant osteotomy preparation, and the samples processed histomorphometrically to assess the fraction of new bone (%NB), residual graft (%RG) and soft tissue matrix (%STM).

Results

- Overall, both treatment groups showed significant reductions in mean RW from baseline to 4 months after extraction, but no significant change in either mean BH or PH over this time.
- When CBCT measurements were analysed according to the initial thickness of the buccal wall (BT < 1 mm vs. BT ≥ 1 mm), significant reductions in all ridge dimensions (RW, BH and PH) were noted in the <1 mm BT group.
- Histomorphometrically, the DBBMC-EMD test group showed significantly increased new bone formation (%NB): (control = 16.5 ± 6.9% cf.; test = 45.1 ± 8.8%) with less residual graft (%RG): (control = 36.8 ± 8.8% cf.; test = 20.3 ± 7.2%) compared to the DBBMC control group.

Conclusions

Both DBBMC alone and DBBMC-EMD treated sites 4 months after extraction lost RW but showed no significant change in BH or PH. Irrespective of treatment, maxillary anterior teeth with thick initial buccal walls (≥1 mm) exhibited less alveolar ridge reduction 4 months after treatment. The addition of EMD to DBBMC resulted in more new bone formation in the test group.

*Adapted from F Mercado et al., Clin Oral Implants Res. 2021 Mar 13, for more info about this publication click **HERE***

Int J Oral Maxillofac Implants. Mar-Apr 2021; 36(2):371-378. doi: 10.11607/jomi.8645.

One-Year Results Assessing the Performance of Prosthetic Rehabilitations in the Posterior Maxilla Supported by 4-mm Extra-short Implants Splinted to 10-mm Implants: A Prospective Case Series

R Gašperšič, M Dard, S Linder, Č Oblak

Study objectives and methods

The aim of this study was to evaluate the survival and success rates of oral rehabilitations in a shortened maxillary dental arch and expanded maxillary sinus with 4-mm extra short implants splinted to longer ones.

One 10-mm and one/two extra short 4-mm titanium-zirconium SLActive tissue-level dental implants were inserted into 11 patients with limited vertical bone availability due to an expanded maxillary sinus antrum. Immediately and 6 months after insertion, implant stability resonance frequency analysis (RFA) values were assessed with an Osstell device. Splinted crowns combining 4- and 10-mm implants were supplied to all 11 cases.

Results

- In 10 cases, the bone quality was type III, and in one case, type IV. Among 17 4-mm and 11 10-mm implants, the median RFA values were 61 (interquartile ranges [IQR]: 59 to 64) and 66 (IQR: 64 to 72).
- One 4-mm implant failed to osseointegrate and was removed. After 6 months of healing, secondary-stability measurements of 16 of the remaining 4-mm implants increased to 68 (IQR: 62 to 72) and of 10-mm implants to 78 (IQR: 77 to 80).
- After 1 year, all (11/11) oral rehabilitations supported by 10-mm (11/11) and 4-mm (16/16) implants were functional.
- The medians and IQRs of the probing depths (median: 2.8 mm, IQR: 2.3 to 3.1 mm vs median: 2.9 mm, IQR: 2.4 to 3.1 mm) and the crestal bone loss (median: 0.75 mm, IQR: 0 to 0.9 mm vs median: 0.22 mm, IQR: 0 to 0.4 mm) for the 10-mm and 4-mm implants, respectively, were similar.

Conclusions

Rehabilitations with splinted crowns combining 4- and 10-mm implants demonstrated a favorable 1-year performance in a shortened maxillary dental arch.

*Adapted from R Gašperšič et al., Int J Oral Maxillofac Implants. Mar-Apr 2021, for more info about this publication click **HERE***

Int J Implant Dent. 2021 Apr 6;7(1):26. doi: 10.1186/s40729-021-00308-z

Single tooth restoration in the maxillary esthetic zone using a one-piece ceramic implant with 1 year of follow-up: case series

M Vilor-Fernández, A García-De-La-Fuente, X Marichalar-Mendia, R Estefanía-Fresco, L Aguirre-Zorzano

FREE FULL TEXT

Study objectives and methods

Oral implants have helped clinicians to improve the quality of life for many patients. The material of choice for dental implants currently remains titanium type IV, whose mechanical and biological properties have been proven throughout the history of implantology. Yet, this material is not exempt from complications. For these reasons, ceramic alternatives to titanium have emerged. Thus, the purpose of this study is to evaluate peri-implant hard and soft tissue stability with the use of a one-piece ceramic implant (Straumann® PURE Ceramic Implant) during 1 year of follow-up.

One-piece all-ceramic zirconia (ZrO2) implants were placed to replace single missing teeth in the esthetic zone. Six to 8 weeks after the procedure, the definitive prosthesis was fabricated. At the time of prosthesis, placement (T0) photographs and periapical radiographs were taken, and the following clinical parameters were recorded: probing depth (PD), plaque index (PI), bleeding on probing (BOP), suppuration on probing (SOP), distance from gingival margin to incisal edge (GM-IE), and Jemt papilla index (JPI). Follow-up appointments were scheduled at 4 (T4), 8 (T8), and 12 (T12) months, when the same parameters were recorded. In addition, plaque control was reinforced, and prophylaxis was carried out. In this last appointment, a final periapical radiograph was taken to assess marginal bone loss.

Results

- A total of 32 zirconia implants were placed in 28 patients (16 women and 12 men, aged between 34 and 67 years).
- The survival and success rate were 96.9%.
- The increase in probing depth from baseline to 12 months was 0.78 mm.
- Assessments of plaque index and bleeding on probing showed a slight increase throughout the study.

Conclusions

The results obtained with the Straumann® PURE Ceramic implants show them to exhibit very good clinical behavior. The survival rate of the implants of our pilot study was 96.9%. For these reasons, we can say that zirconia implants could be an alternative to titanium implants in the esthetic zone.

*Adapted from M Vilor-Fernández et al., Int J Implant Dent. 2021 Apr 6;7(1):26, for more info about this publication click **HERE***

J Int Acad Periodontol. 2021 Apr 1;23(2):115-137.

Immediate implant placement in periodontally infected sites: A systematic review and meta-analysis

J Kaur, G Singh Chahal, V Grover, D Bansal, A Jain

Study objectives and methods

The purpose of this meta-analysis is to systematically evaluate published evidence literature pertaining to report the differences in the survival rate of immediate implant placement in infected sites and non-infected sites.

After the application of the search strategy in PUBMED, SCOPUS, and EMBASE research databases, a total of 1864 papers were found. Titles and abstracts were screened, yielding 77 full-text papers. After the overall assessment, 23 articles were recruited based on the inclusion criteria for analysis of data.

Results

- Out of 23 studies, 14 studies were combined to assess the risk ratio of survival rate of immediate implant placement between infected and non-infected sites, depicting no significant difference on the survival rate.
- Further pooled estimate of proportion of survival rates were 0.98 suggesting 98% survival rate of immediate implants placed in infected sockets when 9 retrospective and prospective studies (no control studies) were combined.
- These findings demonstrate that successful outcomes can be expected for immediate implants when placed into infected extraction sockets.

Conclusions

Within the limitations of this systematic review, equal predictability for successful osseointegration and long-term functioning of immediate implants was found in infected as well as in healthy extraction sites, but astringent antiseptic environment is mandatory for wound healing of immediate implants.

*Adapted from J Kaur et al., J Int Acad Periodontol. 2021 Apr 1;23(2):115-137, for more info about this publication click **HERE***

References

E El Chaar et al., Clin Oral Investig. 2021 Apr 16| **F M Coskunses et al.,** Int J Implant Dent. 2021 Apr 16| **D French et al.,** Clin Implant Dent Relat Res. 2021 Mar 25,| **A Stavropoulos et al.,** Materials (Basel). 2021 Mar 29;14(7):1678 **| J O Abaricia et al.,** Clin Oral Implants Res. 2021 Apr;32(4):487-497| **M A Rausch et al**., Biology (Basel). 2021 Apr 22;10(5):356 | **X Yu et al.,** Sci Rep. 2021 Apr 14;11(1):8152| **F Mercado et al.,** Clin Oral Implants Res. 2021 Mar 13 | **R Gašperšič et al.,** Int J Oral Maxillofac Implants. Mar-Apr 2021| **M Vilor-Fernández et al**., Int J Implant Dent. 2021 Apr 6;7(1):26,| **J Kaur et al.,** J Int Acad Periodontol. 2021 Apr 1;23(2):115-137| source: www.pubmed.gov | Dr Nair holds a position of Global Scientific Communications Manager at Institute Straumann in Basel, Switzerland.

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