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ARE RESTORATIONS MANUFACTURED BY CAD/CAM READY TO FIXATION WITHOUT ADJUSTMENTS?

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Introduction (aim of the study): The master cast is the gold standard for the control and eventual adjustment of restorations produced by conventional procedures. Some digital workflow bypasses the master cast and relies completely on the precision of the CAD/CAM restoration.

The study aims to examine the reproducibility of the margins of CAD/CAM restorations generated from a single digital scan. Also, to check the readiness of these restorations for delivery directly after fabrication without adjustments on the master cast and thereby eliminate the need for the master cast.

Methods: A total of 18 metal substructures made from cobalt chrome alloy were fabricated utilizing a single STL file. The circumference was divided into eight zones. The vertical marginal discrepancy (VMD) was measured at each zone of each metal substructure, with optical microscopy at ×200 magnification.

Results: Measurements of vertical marginal discrepancy were in a range of (−94: 300) with a mean of 62 ± 60 μm. A one-way ANOVA test revealed that the mean VMD is significantly different among the 18 substructures (F17, 1,134 = 63.948, p < 0.001).

Discussion: Although all the received substructures were fabricated from the same scan file, they were not identical and varied widely, and they were going outside the acceptable range in some zones.

Conclusions: Within the limitations of this study, the marginal fit can be improved by extraoral adjustments on the master cast. Thus, skipping the master cast deprives the dentist of delivering a restoration of higher quality.

SOLUTION TO PROTECT ESOPHAGEAL NITI STENT FROM THE CORROSIVE ENVIRONMENT OF THE HUMAN BODY AND NEW APPROACHES IN THEIR TESTING

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Introduction: Due to its properties such as mechanical properties, biocompatibility or corrosion resistance, NiTi alloy is used in a wide range of medical fields from orthodontic wires to spinal clips and stents. A typical use of NiTi stents is to mitigate the impact of esophageal cancer, where the stent causes patency of the esophagus. Corrosion resistance is crucial to ensuring the safety and efficacy of the stent. The key to obtaining relevant information on corrosion resistance is to establish an electrolyte that better reflects the actual environment of esophagus. There is currently no standard that defines the environment for measuring the corrosion resistance of esophageal stents.

Methods: A comparison of different environments. NiTi esophageal stents from 4 anonymized manufacturers (A–D) using 3 types of wires from different suppliers (1–3) were used for the measurements. The samples were exposed in an environment SGF and PBS. Cyclic polarization according to ASTM F2129-19a standard.
2. Influence of input material and production processes on corrosion resistance. The 6-week immersion of stents in SGF was performed. With a subsequent assessment of the surface condition by X-Ray photoelectron spectroscopy (XPS) and scanning electron microscopy (SEM). The amount of ions released from the stents was monitored by atomic absorption spectroscopy (AAS).

Results:
Ad 1
- Breakdown potentials ($E_b$) decrease in SGF and at the same time to an increase in the corrosion current density ($j_{corr}$).
- The integrity of the stents was compromised in the SGF.
Ad 2
- Corrosion initiation occurs on the free surface of the stents and not in the wire crossing
- There was a decrease in nickel concentration from the surface of the stents.
- Stents with a higher concentration of nickel on the surface before exposure release more nickel ions.

Discussion: Based on the comparison of cyclic polarizations, the environment determined by the above-mentioned standard can give distorted results about the corrosion resistance of stents in the esophagus (higher $E_b$ values and lower $j_{corr}$ values in PBS).

The 6-week exposure of the stents shows that the production process significantly affects the corrosion resistance. An inappropriate combination of input material and production process, a significant reduction in corrosion resistance can occur.

Conclusion: From current research, a corrosion testing environment has been established that provides relevant information on corrosion resistance.

From the 6-week immersion, it was found that a poorly chosen combination of wire and production process can rapidly deteriorate corrosion resistance, but also that there is a production process in which the quality of the input material has a negligible effect on the final corrosion resistance of the stent.

THE RELATIONSHIP BETWEEN NUTRITIONAL STATUS AND THE OCCURRENCE OF FRAILTY AND QUALITY OF LIFE IN PATIENTS WITH CHRONIC KIDNEY DISEASE UNDERGOING HEMODIALYSIS – A PILOT STUDY

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Introduction: Chronic Kidney Disease (CKD) is often in Poland disease syndrome classified as a chronic non-com municable disease. Hemodialysis is one of the methods of renal replacement therapy. People with CKD often have abnormal body weight, protein-calorie malnutrition, muscular sarcopenia, and frailty syndrome. The specificity of hemodialysis treatment requires regular visits to the dialysis center, which worsens the quality of life of patients. The main purpose of the study was to define the relationship between nutritional status and the risk of frailty syndrome and quality of life of patients with CKD undergoing hemodialysis (HD) treatment.

Methods: The study was conducted at a dialysis station at a hospital in Katowice with the participation of chronic hemodialysis patients and consisted of a total of 34 patients aged 30 to 90. Men constituted the majority (N = 22) in comparison with women (N = 12). Body Mass Index (BMI), muscle strength, arm circumference, lean body mass after dialysis, adipose tissue mass after dialysis, % of adipose tissue after dialysis and phase angle after dialysis, were measured. Standardized questionnaires KDQOL L.3, Tilburg, were used. An additional research tool was a self-constructed questionnaire containing questions on age, education, place of residence, vascular access.

Results: The study involved 34 patients aged 30 to 90 (M = 63.06; SD = 14.70), treated with HD. As strength increases muscle quality of the examined persons, the quality of life index in the physical area increased moderately functioning and symptom and problem list (p < 0.05). Positive associations of moderate strength occurred also between lean body mass after dialysis and physical functioning, sf 12 mental composite, symptom and problem list, cognitive function, energy/fatigue and role physical (p < 0.05).

Discussion: Other authors also cite the relationship between muscle strength and the quality of life and patient satisfaction (Hoshino, 2021). Malnutrition, in turn, is perceived as the most significant determinant of the quality of life domains of the KDQOL-SF questionnaire (Visiedo et al., 2022). Saitoh et al. (2020) suggested that a lower phase angle value was associated with a higher risk of protein-calorie malnutrition and frailty in HD patients.

Conclusions: The strongest relationship between the nutritional status assessment parameters used in the study and the quality of life domains was obtained between: muscle strength and the quality of the quality of life index in the physical area and functioning and symptom and problem list, between lean body mass after dialysis and physical functioning, sf 12 mental composite, symptom and problem list, cognitive function, energy/fatigue and role physical.

ASPIRIN THERAPY INCREASES LIKELIHOOD OF OPERABILITY AND REDUCES METASTATIC RISK IN PANCREATIC ADENOCARCINOMA

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Introduction: Blood platelets (PLT) are known to support tumorigenesis, angiogenesis and metastasis. Acetylsalicylic acid (ASA) is a known PLT inhibitor and has been shown to reduce cancer incidence, metastatic rates and improve
survival in some cancer types. This study aims to assess the effect of ASA on the clinical outcome in pancreatic ductal adenocarcinoma (PDAC) and determine whether use of ASA may offer survival benefits or therapeutic advantages.

**Methods and patients:** Retrospective analysis of data collected from a cohort of 182 patients with PDAC in a 6-year period was performed. The effects of ASA use for two or more years on operability, TNM stage, overall survival, disease-free survival and time to progression was assessed. Furthermore, the effect of ASA on metastasis in subgroups of patients was evaluated.

**Results:** According to our data, in the group of patients without ASA therapy (non-ASA), 75% presented with inoperable tumours and 57% had metastasis upon diagnosis. Among the patients with tumours localized in the head of the pancreas, 49% had metastases when diagnosed, in non-ASA and ASA group respectively. Similarly, in the subgroup of patients with tumours localized outside the head of the pancreas, 74% in comparison to 33% of patients presented with metastasis at diagnosis in non-ASA and ASA group, respectively. These findings were shown to be statistically significant using logistic regression and age was found to have no correlation with operability or risk of metastasis. We observed no significant difference in either T or N stage between both groups, as well as no significant effect on over-all survival, disease free survival or time to progression using log-rank test.

**Discussion:** In this study, we demonstrate that ASA use is associated with a higher probability of operability. The reason for this finding could be reduction of metastatic spread through the lymphatic route for tumours involving the head of the pancreas, or outside of the head (body, tail and uncinate process). Although ASA treatment did not influence survival endpoints, it may offer clinical and therapeutic advantages and allow a higher probability for presenting in curable or treatable stages of PDAC. Limitation of this study, however, is its single-centred character and relatively small sample size.

**Conclusion:** Our retrospective analysis shows that patients treated by ASA for two or more years were nearly twice more likely to present in operable stages upon diagnosis of PDAC and over two times less likely to present with metastasis.

### HULL'S MAGIC BOX: ARGinine METHYlation INHIBITORS AS A POTENTIAL NOVEL THERAPY FOR GBM

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**Introduction:** GBM tumours are diffuse, necrotic and the most common and aggressive form of glioma in the central nervous system (Louis et al. 2021). Patients undergo the Stupp regimen of surgical resection, ionizing radiation and chemotherapy using temozolomide (TMZ) (Stupp et al. 2009). This has remained unchanged for 15 years and median life expectancy for these patients is around 14 months from diagnosis (Zhu et al. 2017), highlighting the urgent requirement for novel therapeutics. Research into the effect of arginine methylation in GBM has provided new therapeutic targets (Samuel et al. 2021) and protein arginine methyltransferase (PRMT) inhibitors, such as GSK3368715 have recently entered clinical trials for a range of other cancers (Fedoriw et al. 2019) and could be promising new therapies for GBM.

**Methods:** GBM biopsies from Hull Royal Infirmary, or healthy mouse brain tissues, were maintained in a novel fluidics system, pioneered in Hull, for 8-days and perfused with GSK3368715-treated media, at 3 μl/min, mimicking the in vivo environment and synergising with personalised patient care and precision medicine.

**Results and Discussion:** GSK3368715 causes apoptosis of GBM tissue ex vivo but not of healthy tissue. Immunohistochemistry using apoptotic inhibitor cleaved-PARP indicated a 2.17 ± 1.1-fold increase in apoptosis in GSK3368715-treated GBM samples, showing that PRMT inhibition causes cell death in GBM ex vivo.

**Results and Discussion:** RNA-sequencing determined thousands of differentially expressed genes in GBM tissues resulting from GSK3368715 treatment, showing highly significant GO-term-enrichment in ribosome and translation pathways, suggesting decreased protein synthesis capacity after GSK3368715 treatment. My data also indicated a reduction in variation of differentially expressed genes upon PRMT inhibition, from more aggressive to less aggressive phenotypes in principal component analysis. Additionally, several hundreds of genes were found to be undergoing alternative splicing (AS), compatible with a mechanism where changes in the arginine methylation pattern of spliceosome member fused in sarcoma (FUS), upon GSK3368715 treatment, contribute to AS. GO-term-enrichment of these AS events was found in DNA damage and cell death, giving credence to my results which highlight GSK3368715 as a cause of apoptosis in GBM maintained ex vivo.

**Conclusion:** My results highlight an exciting new potential therapeutic target for GBM, via induction of alternative splicing pathways, through arginine methylation inhibition, which may underly the initiation of apoptotic pathways and tumour cell death of a disease with clear clinical needs.
**Introduction:** Type 2 diabetes mellitus (T2DM) is one of the most common diseases in the world. The disease affects all organ systems and, in particular, gastrointestinal. There are some studies, that display such changes in morphology and the functional activity of the gastrointestinal tract. For instance, atrophy of the gastric mucosa, antibodies to parietal cells, a decrease in tone and motility, abnormalities in the vessels of the villi, and microbiome misbalance. The influence of T2DM on the gastrointestinal tract is generally studied, although, the changes in the functional activity of stomach granulocytes are insufficiently studied. Therefore, the aim of the study is to observe the changes in the mucin secretion of the gastric mucosa of rats against the background of the course of diabetes mellitus 2 and its correction by the combination of metformin with propionic acid.

**Methods:** T2DM was simulated by streptozocin injections and food challenge in 24 white laboratory rats, which were divided into 4 groups: the 1st group – T2DM without treatment, the 2nd group – T2DM + metformin, the 3rd group – T2DM + propionate, and the 4th group – T2DM and metformin + propionate. The group received drugs for 14 days. For histological examination, the stomach was taken for histochemical examination. Statistical data processing was done using the StatPlus program ver. 7.3.0. The difference between groups was considered significant at p ≤ 0.05.

**Results:** The gastric glands of rats from the control group had the localization of mucin both on the surface and in the cells. There are mucopolysaccharides in all parts of the fundal glands. The 1st and the 2nd groups had similar changes, which included the reduction of mucin in the cells by 2.6 times compared to the control, and mucopoly saccharides were not found in the deep parts of the glands. In the 3rd group against the background of treatment by propionate are increase in mucin synthesis by 25% (p ≤ 0.05) was observed in comparison with the indicators of the 1st, 2nd, and 4th groups. However, the amount of mucus-producing cells also increased in the 4th group that used the combination of metformin and propionic acid. It is believed that a sharp decrease in the amount of mucin occurs as a result of inhibition of the activity of synthetic processes and, in particular, glycoproteins, against the background of type 2 diabetes.

**Conclusions:** A significant decrease in mucin production in the base of the gastric glands of rats by 2.6 times was established, which is associated with a decrease in the number of cells producing mucopolysaccharides. Metformin did not affect the increase in the production of mucin in the stomach in patients with type 2 diabetes, but the use of propionate both alone and in combination with metformin increased the production of mucopolysaccharides.

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**THE EFFECT OF THE COMBINATION OF TEMOZOLOMIDE AND FLUBENDAZOLE ON GLIOBLASTOMA CELLS**

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**Introduction:** Glioblastoma multiforme (GBM) is the most common and malignant primary brain tumor. Infiltrative growth, many different genetic and epigenetic variants as well as low plasma concentration of the alkylating drug temozolomide (TMZ) in the tumor and quickly developing chemoresistance are the reasons of therapy failure.

One of the strategies of increasing the treatment effectiveness is to combine drugs with different mechanisms of action. Flubendazole (FLU), the member of benzimidazole group, exhibits anticancer effect based on its ability to interact with cell microtubules. Cell microtubules play important role in proliferation and invasion of cancer cells. Higher expression of βIII-tubulin found in higher grade gliomas indicates possible treatment target.

The aim of this study was to investigate the effect of the combination of TMZ and FLU on the viability and survival of stabilized GBM cell lines (A172, T98G and U118MG) and to verify this effect in an in vivo model.

**Methods:** Cell viability and proliferation were evaluated biochemically (WST-1 assay) and cytometrically (phase contrast microscopy). Drug synergism was determined using CompuSyn software. Changes in microtubule morphology were examined by fluorescence microscopy. Quantification of TMZ, FLU and their metabolites in cells was carried out using LC/MS analysis, while expression of selected cell cycle markers was determined by RT-PCR and Western blot.

**Results:** The combination of TMZ and FLU decreased cell viability and proliferation in exposed cell lines more effectively than with individual drug. Furthermore, changes in cell morphology and microtubule structure were notable as well as differently expressed cell cycle markers, such as cdc2 or cyclin B. Use of this combination also increased the amount of TMZ and FLU accumulated in tested GBM cell lines as well as in the tumor and brain of in vivo model organism.

**Discussion:** In our study, we combined the commonly used chemotherapeutic drug TMZ and a candidate anticancer drug FLU, which fits in a currently used concept aiming the improvement of the treatment efficiency in various types of cancers. Our obtained data clearly demonstrate improved efficiency of our drug combination in vitro and in vivo GBM models. Since the use of tested drug combination also resulted in an increase of drug accumulation in GBM cells, this strategy should be the subject of further investigation.

**Conclusions:** Our results demonstrate that FLU improves TMZ antiproliferative effect in all tested GBM cell lines. Moreover, this drug combination caused significant changes in cell morphology, microtubule cytoskeleton and drug accumulation in cells. Obtained results indicate...