**13. PROPOSED RESEARCH PROJECT**

**This template applies to the following Area of Project\* –**

**• Public health, human health and health services research**

**• Infectious diseases**

**• Advanced medical research**

**Please refer to paragraph 13 of *Explanatory Notes – Grant Application for Investigator-initiated Projects* for details of the format. The order of the items listed below should not be altered.**

***\*For health promotion project, please use the health promotion template.***

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|  | Title: | |
|  | A multi-centre prospective validation of ‘MSKalign’ digital low back pain management platform enabling AI auto-evaluation, personalized physiotherapy prescription, and dynamic disease progression prediction | |
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|  | Introduction: | |
|  | 1. Background   The COVID-19 Pandemic has significantly impacted the conventional clinical management of spine diseases. Lack of in-person consultations showed a real need for virtual evaluation and telemedicine.1 This demand remains constant beyond COVID as the waiting time for receiving consultation and therefore being evaluated by spine specialists for further treatment planning is steadily increasing.1 We developed the musculoskeletal alignment (MSKalign) digital management platform for low back pain in this direction with auto-evaluation and personalized treatment planning.  Low back pain (LBP) is the most common cause of years lived with disability worldwide. Between 1990 and 2015, the global years lived with disability caused by LBP increased by 54%.2,3 Despite the high prevalence of LBP, approximately 90% of LBP cases have unknown etiology and are diagnosed with non-specific LBP. Although most people with LBP recover quickly, many experience recurrent LBP and some develop persistent pain and disability.4 While LBP is not a life threatening health condition, the costs of LBP are comparable to other prevalent, high-cost conditions (e.g., cardiovascular diseases), and are associated with healthcare consumption and reduced productivity.3,5 Disability caused by LBP is projected to continuously increase in coming decades given an ageing and increasingly inactive population.3  LBP is particularly common with 21% of individuals in Hong Kong reporting LBP in the past 12 months.6 The diagnosis process is complex as multiple possible pain generators may exist in the same patient. Up to 90% of these back pain cases may actually go on to pain relief modalities without a clear diagnosis only to be compiled into a general umbrella term of “non-specific low back pain”.7 Hence, personalized treatment for patients becomes a difficult task for clinicians to achieve expected outcomes. Here, an AI-driven platform first **automatically identifies** patients whose LBP has a pathoanatomical cause thats need potential surgical intervention, then **customizes the physiotherapy (PT) plans** consisting of educational material, self-management exercises, and psychotherapy for patient with **non-specific LBP**.  Recent advancement in information and communication technology (ICT) places strong emphasis on supporting self-management programs for chronic pain through mobile software apps.8,9 Mobile apps have been identified as a way to reduce the financial burden of chronic neck and back pain.10 Use of ICT as part of rehabilitation programs has been suggested to increase adherence to self-management programs.11 The personalized PT plan prescribed by MSKalign includes tailored educational sessions and specific exercise training in line with patients’ goals, personal characteristics, symptom progress, and degree of disability. The exercise plan conveyed to patients includes instructions and videos demonstration of the exercises along with recommendations for the number of sessions per week and repetitions or sets within a session. Educational material about the pathological causes of back pain, the natural course of LBP, pain physiology, principles for using exercise to manage back pain, and coping strategies are provided for the users on the MSKalign platform.  Our current MSKalign platform (Figure 1) has been **preliminarily tested at the spine clinics** of Queen Mary Hospital at patients’ mobile devices (including smartphones and tablets). Spine specialists at MacLehose Medical Rehabilitation Centre, Queen Elizabeth Hospital and Pamela Youde Nethersole Eastern Hospital have also had the application installed on their devices and provided written supporting document for collaborating with us on the prospective validation study of the platform. Clinicians from the participating centres had long history in collaborating with Queen Mary Hospital by exchanging surgeons for training and communication in the past years. Since the early development stages of MSKalign, spine specialists and physiotherapists from participating medical centres worked together to develop the educational material and basic movement patterns included in the PT plans.   1. Technical Novelty Capacity   We have achieved AI auto-evaluation of the causes of LBP based on structural data collection through dynamic questionnaire and motion analysis through 3D pose detection. Our AI model can **automatically classify** patients into two groups: LBP patients with a pathoanatomical cause, who thus need **immediate medical attention**, and patients who had back pain for unspecified reasons (non-specific LBP), who will be provided with **digital** **self-management plans** on the MSKalign platform.  Further, our MSKalign platform provides personalized PT planning that can be delivered on mobile device, by adapting the **case-based reasoning (CBR)** technology (Figure 2), a knowledge-based approach relying on a case library of past experiences to tailor a personalized PT plan for new patients, enabling a patient-centreed intervention based on what has and has not been successful in previous patient cases. Having easy access to tailor-made pain management plans will help increase patient adherence to the rehabilitation process. When more follow-up data are collected, we plan to optimize and update personalized exercise programs using **generative AI models** such as Variational Autoencoders (VAE) and Generative Adversarial Networks (GAN).12,13 Generative AI models are based on machine learning algorithms that can identify patterns and relationships in the input data to create new, personalized exercise programs for the management of low back pain. While CBR typically requires less training data than generative AI models, the latter is capable of updating the personalized PT plan constantly based on patient feedback, including symptom updates and adherence to the exercise plan. Throughout the personalization process, physiotherapists can actively customize the details in the PT plan, incorporating their expertise into pain management.  In addition, dynamic disease progression prediction is achieved with the support from the model trained from our collected dataset. Based on **continuous tracking** on the mobile device and individual-specific pain response to the initial PT plan, modifications of the initial plan can be automatically updated during the follow-up and the disease progression prediction will be updated correspondingly.   1. Future clinical significance   Integrating the currently advanced mobile communication technologies with AI, we have developed and technically tested MSKalign. A prospective clinical validation of the platform is required before it can obtain regulatory approval and have a wider application in providing a ***fully automated, easily accessible, comprehensive and accurate LBP management platform.*** User-friendly interface designed together with our spine surgeons to meet their clinical needs, combined with a standardized acquisition of pain intensity, health-related quality of life (HRQoL), and mental health evaluation longitudinally, this platform can assist in reducing the clinicians’ workload and the patients’ anxiety in waiting for been examined, improving the clinical flow for LBP. In the future, utilizing more data collected through our platform, we will be able to train further improved generative AI models for more accurate auto-evaluation of LBP and self-adapting personalized PT plans, which will benefit the health system of Hong Kong in delivering better care to the patients. | |
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|  | Aims and Hypotheses to be Tested: | |
|  | 1. Aim and objectives   The aim of this study is to clinically validate our MSKalign LBP mobile management platform in four clinical centres, with standardized information acquisitions, AI auto-evaluation, personalized PT planning and disease progression prediction.  Objective 1: to establish MSKalign as an accurate auto-evaluation tool via a multi-centre prospective trial between four spine centres in Hong Kong.  **Milestones:**   1. Recruit 800 participants at the baseline with 200 patients recruited in each centre. 2. Accomplish a dataset with paired patient baseline information and spine specialists assessed causes for LBP (pathoanatomical versus non-specific) as ground truth (GT) measurements. 3. Achieve high agreement comparison between the **MSKalign predicted cause for LBP** and the GTs (sensitivity>0.95 and negative predictive value>0.95).   Objective 2: to validate the clinical outcomes of MSKalign as an AI physiotherapy platform in comparison with conventional manual physiotherapy prescriptions.  **Milestones:**   1. Collect a dataset with 250 patients who managed LBP using intervention in the conventional clinical setting with 6 months follow-up. 2. Collect a dataset with 250 patients who managed LBP using digital PT plans prescribed by MSKalign with 6 months follow-up. 3. Achieve comparable **treatment responses** (improvement in pain intensity, health-related quality of life (HRQOL), disability score, anxiety and depression score) using either conventional PT or MSKalign (*Concordance correlation coefficient >0.85 and absolute mean error<0.5* via linear regression and Bland-Altman plots).   Objective 3: to investigate the accuracy of MSKalign for LBP progression/recovery prediction.  **Milestones:**   1. For 250 LBP participants who completed follow-ups and utilised MSKalign PT plans, compare the **AI disease progression prediction** with the patient reported disease progression. The main indicators for disease progression are pain intensity and disability score. 2. Fine-tune MSKalign with local data to improve the prediction accuracy of individual-specific disease progression to achieve an accuracy of 75% in comparison with the self-reported LBP recovery progression. 3. Hypotheses   We hypothesize that MSKalign has high sensitivity in detecting and accurately evaluating LBP that may require medical attention and can provide sufficient personalized PT plans for individuals, as well as high sensitivity in predicting subject-specific disease progression using baseline information.  Sub-hypothesis 1: The sensitivity of MSKalign in detecting LBP with pathoanatomical causes is >95% to trigger prompt interventions, whereas the negative predictive value of MSKalign in detecting the disease is >95% to avoid unnecessary clinical interventions.  Sub-hypothesis 2: The digital intervention schemes prescribed by MSKalign has no reduction in outcome delivery compared with conventional PT treatment.  Sub-hypothesis 3: The disease progression prediction by MSKalign can achieve 75% accuracy in comparison with the self-reported LBP recovery progression. | |
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|  | Plan of Investigation:  [For advanced medical research, basic/pre-clinical research studies are not supported. Please state clearly how the study will focus on clinical studies and apply advanced technologies to facilitate the translation of knowledge generated from health and health services or infectious diseases studies into clinical practice and to inform health policies.]  [For project addressing the thematic priority of Implementation Science, please state clearly the proposed framework(s) / model(s) to analyse barriers and facilitators of implementation outcomes.]  [For seed grant application (i.e. grant ceiling is HK$500,000), please state clearly the pre-set criteria to enable scale-up to a larger project and/or enhance the efficacy/effectiveness of existing practice.] | |
|  |  | Subjects (with justification on the sample size)  All adult patients with LBP at the four collaborating centres who meet the following eligibility criteria will be recruited:  *Inclusion criteria*   1. Male and female patients who are 18 to 65 years old with LBP. 2. Able to understand the nature and scope of the study and provide written consent for their data to be re-used for research purpose. 3. Have a mobile device (including smartphones or tablets) that can download MSKalign.   *Exclusion criteria*   1. Patients will be excluded if they are diagnosed with or have any signs of psychological disorders that may influence the compliance of the study. 2. Patients will be excluded if they have any pre-diagnosed systematic neural disorders that may influence the mobility of the patients (e.g. prior cerebrovascular accident, Parkinson’s disease, myopathy). 3. Patients will be excluded if they have the following musculoskeletal diseases:  * Congenital spinal deformities, * McCune-Albright syndrome, * Early-onset scoliosis, * Previous spine operations and instrumentation performed, * Trauma that may impair posture and mobility, * Adolescent idiopathic scoliosis (AIS), and patients who have brace treatment for AIS before.  1. Patients will be excluded if they have any oncological diseases. 2. Patients will be excluded if they have any other systematic diseases. 3. Patients will be excluded if the patient cannot complete the consent process. 4. Patients will be excluded if the patient and the carer do not have access to smartphones, and/or unable to attend training sessions for using the mobile platform. 5. Patients who have any medical conditions that preclude physical activity or exercise will be excluded as they may not be able to participate in the intervention. 6. Patients who are currently pregnant or planning to become pregnant during the study period will be excluded.   The sample size is estimated based on our pilot results for LBP source classifications. The pain cause classification error was 0.086 as we tested in our local centre on 31 participants. When we choose a power of 0.95 and an effect size of Cohen’s d=0.5, a sample size of 130 is sufficient to validate our model. However, we intend to cover the true classification error of the model on unseen data via a multi-centre setting, thus we proposed total sample size of 800 with each centre recruiting 200 participants. The proposed sample size exceeds the required sample size to validate our model.  The patient number in Objective 2 was estimated based on the clinical volume and the recruitment capacity at 4 centres as treatment and follow-up periods are involved. Currently, 150-200 patients per week visit each spine centre. Assuming more than ½ are new patients and ¼ of the new patients meets with the inclusion and exclusion criteria and agrees to participate, we can recruit approximately 20 patients every week at each centre. With 28 weeks and 4 collaborating centres, we will have more than 2200 eligible participants at the baseline. According to our study design, eligible participants will go through a 6-month intervention period and a 6-month follow-up period. The sample size assumption is based on the single centre testing study at our local centre of the MSKalign platform. In our single centre testing, over ¼ of the patients are compliant with the intervention programs. Assuming more than 2200 eligible participants can be recruited as the baseline, we set the sample size for objective 2 at 500. |
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|  |  | Methods  *Patient recruitment and follow up*  The spine clinics four participating spine centres at 1) the Queen Mary Hospital, 2) MacLehose Medical Rehabilitation Centre, 3) Queen Elizabeth Hospital, and 4) Pamela Youde Nethersole Eastern Hospital run 1-2 times on a weekly basis. All patients visiting our spine specialist collaborators of this study will be invited for study.  Upon written consent being received from the patient, three sections of digitalized clinical information collection will take place, 1) patient’s self-input on our user-friendly interfaces with dynamic questionnaire, 2) medical staff’s input for physical examinations, 3) Automatic 3D pose assessments performed by our AI system.  MSKalign digitally analyzes whether a patient’s LBP is pathoanatomical or non-specific through the following steps. First, when a patient first enters the clinic deployed with MSKalign, they are presented with a user-friendly interface that prompts them to enter their baseline information that can be used for LBP auto-evaluation. **A set of dynamic questionnaires** has been designed for data collection. Based on the answers to each questionnaire provided by the patients, the order and the presence of the questionnaire will change accordingly. Demographic data, pain level, onset, treatment history, and daily activities are recorded. Hospital Anxiety and Depression Scale (HADS) questionnaire will be used to measures anxiety and depression, while a red flag screening questionnaire detects underlying conditions needing urgent attention. Second, the results of **a series of physical examinations** performed by clinicians will be recorded on the MSKalign platform, including pain-triggering movements, pelvic inflammatory disease screening, and neurological disorder screening. Tests may evaluate reflexes, myelopathy signs, and lower limb myotomes. Joint range of motion and local tenderness are assessed, with results entered into appropriate fields on the platform using clinician credentials. Third, MSKalign integrates **3D pose detection technology** and **AI key point detection** to assist with the evaluation tasks, such as measuring a patient’s joint range of motion and performing scoliosis screening. Using lumbar range of motion as an example, clinicians can use a mobile device with a camera to record videos of patients’ lumbar flexion and extension movements, calculating range of motion with pose tracking algorithms. Further, our previously developed AI models can analyze the images to detect malalignment of the spine and accurately calculate the cobb angle based on bare back image along.14,15 After the digital analysis, a clinician will use conventional paperwork to analyze the same patient blinded to the digital analysis. After the LBP assessment, participating patients will be assigned to either the conventional PT plan group or the digital PT plan group.  Once the patient is evaluated to have non-specific LBP without a pathoanatomical cause, MSKalign provides personalized PT planning that can be delivered on mobile device. While following the personalized PT plan that typically last 3-6 month, MSKalign platform also serves as a **follow-up tracking tool**. The patients will be able to update their treatment responses, including disability score, pain intensity, health-related quality of life (HRQOL), anxiety and depression score on MSKalign platform. Based on these continuously updated individual-specific pain response to the initial personalized PT plan, the initial plan can be continuously modified during the recovering process. Simultaneously, the disease progression prediction will be updated correspondingly. Based on our preliminary study with an 80% patient retention rate, we assume more than 50% of the patients to be able to complete the follow-up during the period of our study. This leaves at least 400 follow-up cases. The reason that Queen Elizabeth Hospital and Pamela Youde Nethersole Eastern Hospital were selected to join the study is because they have a systematic follow-up protocol similar to Queen Mary Hospital and MacLehose Medical Rehabilitation Centre.  *Assessments and PT plan by clinicians (blinded to the MSKalign results)*  To evaluate the accuracy of MSKalign as an auto-evaluation tool, we will first obtain clinicians’ assessment results of the patients’ LBP as either pathoanatomical (caused by a potentially sinister cause) or non-specific (no specific anatomical cause of pain can be determined). Pathoanatomical cause for LBP includes compression fracture, spinal stenosis, visceral disease, tumour or metastasis, and infection. The assessment results will be recorded as ground truth and compared with the results from digital analysis. A spine specialist will evaluate the potential underlying cause of a patient’s LBP based on the results from dynamic baseline questionnaires, physical examination results and 3D pose detection findings.  For patients assigned to the conventional PT plan group after the randomization process, the clinicians will provide intervention recommendations that they think fit the patient’s current situation. Patients will take medications and attend PT sessions normally. Their treatment responses (improvement in pain intensity, HRQoL, disability score, anxiety and depression score) will be compared with patient in the digital PT plan group.  *MSKalign auto-assessments, auto-plan and progression prediction (blinded to the clinician’s assessments)*  Following our built-in guidance of the data acquisition, the results from dynamic questionnaires, physical examinations, and 3D pose detection will be recorded on the mobile devices deployed with MSKalign and automatically assessed on the platform.   1. *Technical details*   Auto-evaluation of LBP on the MSKalign platform is achieved using a multi-layered perceptron artificial neural network (MLP-ANN) (Figure 3). Specifically, various patients’ characteristics (e.g., demographic data, physical examination results, prior spinal surgery, medication history) and the final classification results (LBP with pathoanatomical causes versus non-specific LBP) in a training database consists of 450 patients was used to train the deep learning model. The neural network processes the patients’ characteristics in hidden nodes and layers based on weights adjusted during training. The weights were adjusted continuously using the training dataset to unveil patterns so that better predictions of patients with correct classification can be made.  MSKalign constitutes a data-driven, predictive system that uses the CBR methodology to capture and reuse patient cases to suggest the most suitable self-management plan for an individual patient. The CBR system in MSKalign interacts with a knowledge repository to suggest a personalized plan for self-management. First, the data collected by the baseline dynamic questionnaire, physical examination, and 3D pose detection are formatted an individual patient case. The best matching case will then be selected to be fitted to the current patient. A core method in this step is **similarity assessment**, which compares how similar cases are to each other on demographic, pain, and mood-related information. After retrieving a similar past successful case, a plan for self-management will be adapted to the current case. This process is guided by a set of adaption rules and the goals set by patients. To enable continuous updates to the self-management plans, the CBR system makes revision to the generated plans as new case takes place. Besides situation-specific knowledge handled by CBR, elements of the model- and rule-based reasoning are also used to capture and utilize generalized knowledge (eg, clinical guidelines) in the plan customization.  For disease progression prediction, a new model is developed based on Long Short-term Machine (LSTM) (Figure 4), a specific recurrent neural network (RNN) that not only has the advantages of an RNN but also has a selective memory function that can be used to prevent gradient disappearance problems16,17. Figure 4 shows the neural network model developed for this project, the input which was derived from data collected through baseline dynamic questionnaires, physical examinations, and 3D pose detection. The model uses an LSTM-based residual learning framework (ResNet) to add time-varying jump connections18, as the deeper neural network provides better performance for model training. The model also applies the back propagation in time (BPTT) algorithm and chooses to mean square error (MSE) as the loss function to improve the efficiency of the model. The final outputs of the model are pain intensity and disability scores.   1. *Technical validation results*   We have preliminarily performed the technical validations of MSKalign to show that the data collected on MSKalign is reliable and accurate.  The MLP-ANN used to classify LBP was validated by evaluating the accuracy of the model in successfully classifying patients with and without a pathoanatomical cause based on a test dataset. The test dataset with 31 patients recruited in a preliminary study between January 2022 and June 2022. The accuracy of the model was checked against the actual medical records that determine the correct classification. A visualization of the neural network’s performance using the confusion matrix indicated that the negative predictive value for non-specific LBP was 1 (Figure 5). With the clinician’s assessment results as the gold standard, our model with high sensitivity based on baseline information has clinical implications in assisting clinicians with fast, consistent, and accurate evaluation of LBP. 800 recruited participants at the baseline with paired patient baseline information and spine specialists assessed causes for LBP will provide a reliable reference point for evaluating the accuracy of the MSKalign platform. In addition, a significant increase in the volume of patient data available for the training of the MLP-ANN will allow the neural network to learn from a more diverse range of patient characteristics and improve its ability to accurately classify LBP into pathoanatomical causes or non-specific LBP. The large dataset will enable us to fine-tune the MLP-ANN by adjusting the weights and biases of the MLP-ANN to improve its ability to accurately classify LBP cases.  Linear regression and Bland-Altman plots were used to validate the reliability of data acquisition on our platform in comparison with conventional methods. Questionnaire scores (pain intensity, HRQoL, disability score, anxiety and depression score) collected through electronic questionnaires on MSKalign and through the conventional questionnaires has been compared and validated. Based on the results from our preliminary study, pain intensity scores collected by electronic and conventional questionnaires show a strong correlation (R2 = 0.981) with a mean difference of 0.100 (CI: -0.580 to 0.780) (Figure 6). Further, quantitative results including lumbar range of motion measured by 3D pose detection have been compared with clinicians’ estimation in the clinic. Based on our preliminary study, lumbar spine range of motion in flexion and extension collected by 3D pose detection and conventional physical examination show strong correlations (flexion: R2 = 0.88, extension: R2 = 0.92) with mean difference of 4.16 degree (CI: 2.75 to 6.24) for flexion and 2.75 degree (CI: 1.35 to 4.03) for extension. |
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|  |  | Study design  The study design is a multi-centre prospective cohort study. All patients attending the spine clinics at four spine centres 1) Queen Mary Hospital, 2) MacLehose Medical Rehabilitation Centre, 3) Queen Elizabeth Hospital, and 4) Pamela Youde Nethersole Eastern Hospital that meet our inclusion and exclusion criteria from the January of 2024 to December of 2024 will be recruited. From our experience in our local centres and our collaborating spine centres, on average 30 patients each week attending the clinical meet our criteria. Thus, 6 months of recruitment in the first year of the study period should be adequate for 1000 participants. The collaborating surgeons will perform routine clinical assessments of the recruited patients in their clinic before the MSKalign auto-assessments, and then the surgeon’s assistants will perform the MSKalign auto-assessments blinded to the consulting surgeon of the patient.  Primary outcomes:  1) Accuracy of MSKalign as an auto-evaluation tool for LBP, measured by the agreement between the MSKalign predicted cause for LBP and the ground truth measurements.  2) Treatment response of patients managed with MSKalign compared to conventional manual physiotherapy, measured by improvement in pain intensity, health-related quality of life, disability score, anxiety score, and depression score.  Secondary outcome:  1) Accuracy of MSKalign in predicting disease progression/recovery for LBP, measured by the agreement between the AI disease progression prediction and the patient-reported disease progression. |
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|  |  | Data processing and analysis  All results from dynamic questionnaires, physical examinations, and 3D pose detection data will be sent to the HKU server for secure storage at the Department of Orthopaedics and Traumatology with authorized access only. When the follow up is completed, the data will be unblinded for comparisons between the clinician GT assessments and MSKalign auto-assessments and evaluation of the prediction accuracies. These results will be analyzed separately for the patients with acute or chronic LBP accordingly to the duration of their conditions.  The LBP classification accuracy of the objective 1 will be tested using the ROC curve and the confusion matric for the classification accuracy based on patient baseline information, in comparison with the clinician’s evaluation results. **Sensitivity** and **negative predicted value** will be calculated using equation (1) and (2).  (1)  (2)  In addition to the sensitivity and the negative predicted value we will also report the **specificity** (true negative rate) and the **positive predicted value** (precision). However, we focus on improving the results of the sensitivity and the negative predictive value because clinically our platform needs to be able to promptly detect red flag symptoms to trigger early emergency interventions, but at the same time to avoid unnecessary surgical interventions.  To compare the **treatment** **responses**, including self-reported pain intensity, disability score, HRQoL, and anxiety and depression score, as a result of personalized PT plan prescribed by MSKalign and the treatment response as a result of the conventional PT treatment. Although patients will be aware of the nature of their PT plans (conventional or digital), the researcher conducting data analysis will be blinded to the intervention. Linear regression and Bland-Altman plots will be used to test the agreement between the treatment responses to personalized PT plan and treatment response to conventional PT. Taking pain intensity (PI) as an example, the slope of the regression line will be assessed with a perfect match value being 45° and the concordance correlation coefficient being 1 indicating a perfect match. The significance level will be determined at p value <0.05. Bland-Altman analysis is a common method to compare the agreements between the two measurement results. The difference between and will be plotted against the average of these two measurements [()/2]. The range of the mean differences and the overall mean differences can be examined, with a value equal to 0 being a perfect match.  In addition, the accuracy of **disease progression prediction results** will be accessed based on patient self-report results (improvements in pain and disability score) during the follow-up period. Statistical measures such as sensitivity, specificity, positive predictive value, and negative predictive value used. **Accuracy** will be calculated using equation (3).  (3) |
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|  |  | Potential pitfalls and contingency plans  1) During the baseline and follow up phases, the collected data may suffer from missing assessment parameters. We have also prepared to accommodate missing parameters by using tensor completion. Further, we plan to use the participants with completed assessment parameter to fine tune and validate the platform.  2) One potential pitfall in this study is the possibility of participant drop-out during the follow-up phase. In our single centre testing, over ¼ of the patients are compliant with the intervention programs. Thus, to achieve the sample size of 500 for objective 2, we aim to recruit more than 2200 eligible participants at the baseline. In addition, we will implement strategies to minimize drop-out, such as providing reminders to participants, offering incentives for completion of follow-up assessments, and maintaining regular communication with participants. In the event of participant drop-out, we will conduct sensitivity analyses to assess the potential impact on the study outcomes.  3) Another potential pitfall is the possibility that new developments in AI methodology may not lead to improvements in classification accuracy. To mitigate this risk, we have built a robust AI framework that allows for flexibility and adaptation to incorporate new developments. We will continuously monitor advancements in AI technology and assess their potential applicability to improve the accuracy of the MSKalign platform. If needed, we will collaborate with experts in the field to update and enhance the AI algorithms used in the platform.  4) Patients in digital PT plans groups who report significantly worse pain in a short period of time will be called back for immediate attention. |
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|  | Existing Facilities: | |
|  | **MacLehose Medical Rehabilitation Centre** (MMRC) is a rehab and long-term care hospital above Sandy Bay in Hong Kong. Founded in 1984 by the Hong Kong Society for Rehabilitation, it has 150 medical rehabilitation beds, including 20 beds for day rehabilitation service. The LBP clinic runs once a week at MMRC with approximately **180 patients seen per week**. Approximately 2500 cases of LBP are seen per year with 300 being new referrals. As a university unit, we have a standardized methodology for imaging and follow-up. **Queen Mary Hospital** is the flagship teaching hospital of the University of Hong Kong with the main specialty clinic covering all adult spine conditions in the cluster. Two other centres (**Queen Elizabeth Hospital and Pamela Youde Nethersole Eastern Hospital**) both had long history in collaborating with Queen Mary Hospital by exchanging spine surgeons for training and communication in the past years. Their spine clinics run once to twice a week with **around 150-200 patients** attending the clinic (of which **½ -¼ are for follow up**). The surgeons participating in this study are qualified spine surgeons with over 10 years of clinical experience. For each centre, two surgeons will be participating in the study. One senior consultant and one junior consultant.  We are fully capable of completing this study as we have already ***completed the crucial steps of implementing and training AI models based on different neural networks*** *for the LBP auto-evaluation****.*** The published studies ***showed our ability to utilize AI to solve real clinical problems***. With a prospectively collected LBP cohort,19 We have conducted deep learning investigation and technical innovations.20 Previously, we have developed AI-embeded telehealth platforms for adolescent idiopathic scoliosis21 and have achieved disease progression prediction.22 The overall technical pipeline can be easily transferred for the current LBP management platform.23 Upon the validation of our platform, clinicians can be provided with an **unbiased** and **easily accessed** tool for individual-specific management.24 Hence, maximizing our potential for preventing disease progression by screening the ones at the risk promptly as well as follow up with regular updates and no necessity to physically attend the clinics/hospitals.  This study focuses on the clinical validation of our existing leaning based system. Our research team have sufficient experience with conducting randomized controlled trials with HMRF support as well (#05161356, #13142371, #05162056). The study investigators include surgeons who are international leaders and pioneers in the field of spine surgery and have extensive experience in conducting large-scale studies and computer scientists who are expect in computer vision. Hence, with this solid multi-disciplinary team framework in place to facilitate this study, this study can be completed successfully with international impact.  We have obtained ethics approval at the Hospital Authority (IRB Ref #: UW-22-270). The collaborating surgeons at the other three centres are processing their ethics approvals. | |
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|  | Justification of Requirements: |
|  | It is likely that physicians will incorporate telemedicine into health care delivery services even after the COVID-19 pandemic subsides because of telemedicine's efficiency in meeting patient needs. This is the direction the Hospital Authority is taking to also lessen the burden of increasing number of patients with these spine conditions. Using the standard maneuvers provided in our study, spine care providers can perform a nearly comprehensive spine examination through telemedicine. This study is critical to validate the reproducibility and reliability of our methodology at different spine centres. As this is a prospective clinical validation trial of our AI model, we will require a longitudinal follow-up of our patients to determine the ability of our platform in generating intervention recommendation and detecting subject-specific pain response in these patients.  The coordination of data acquisition and management will include data entry, appointment management, and results analysis. At each centre the collaborating surgeon and the surgeon’s assistants are going to conduct the data collection with no extra cost. Thus, only two research assistants are required for screening the participant eligibility and good attention to details with basic database experience will be required for the data collected form all four centres. The proposed salary levels are the minimum market value for such personnel. We hope our reputation and the impact of our work would increase our chance of hiring such personnel.  One senior research assistant (HKD549864 for 24 months) will be managing, cleaning and organising the whole dataset (incl. specialists’ GT measurements and the MSKalign auto-assessment results) from four centres participating in this multi-centre trial. Thus, the volume of the data and the workload is significant. To avoid mishandling of the data, experienced personnel for this task is required. The other research assistant (HKD229824 for 12 months) with be mainly performing auditing of the organised dataset. A bio-statistician (HKD114912 for 6 month) will be perform data analysis and drawing insights for LBP using the dataset.  Other expenses proposed under this project mainly including conference (HKD10000 for 24 months) and publication costs (HKD20000). It is followed by a required auditing fee of HKD5000.  No equipment needs to be purchased for our project, because an AI server with 8\*GPU are supported by our ITC and AOSpine projects for the development of this platform that can be continuously used for further prospective clinical validation studies.  For the advisory cost, we plan to seek advice from one external AI modelling professor to provide advice to PI and the project team. In addition to the “AI model fine-tuning” process in the third year of the project, the external AI modelling professor will provide advice regarding standard database structure that can be used for AI training throughout the process of database establishment. He/she will provide guidance in the following practices: 1). Checking the data structure regularly to ensure our database follows the FAIR (Findable, Accessible, Interoperable, and Reusable) guiding principles for data stewardship and management. 2). Assisting in developing standardized code and an application programming interface (API) to access the AI models for validation across different sites. 3). Ensuring data safety by de-identified the data and stored data in a HIPAA-compliant environment with safeguards against data unmasking. The monthly advisory cost is around $4,150, which makes yearly advisory expense $49,800. The total advisory expense should be $149,400.  Upon the completion of the follow-up period, we plan to provide $30 cash for the transportation cost. Assuming 500 patients come back for follow-up evaluation, $15,000 will be used as incentives. |
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|  | Plan to Disseminate Research Findings to End Users: |
|  | Upon the completion and publication of the results of this clinical trial, we provide the spine specialists and the patients with a completely new LBP management platform with auto-evaluation, personalized PT planning and dynamic disease progression prediction. The platform will continuously benefit spine specialists and patients internationally as it can provide them with fully automated, fast, unbiased, and comprehensive analysis of LBP. With clinical validation, the platform developed in Hong Kong will have the potential to become the future gold standard for LBP assessment and follow-up. Due to the automated system and accurate AI detections, it can potentially reduce the cost of the public health system and significantly improve the patients’ clinical experience providing real-time and continuous feedback. |
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| h) | Key References: |
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