Enhancing the Therapeutic Effect of Bracing for Adolescent Idiopathic Scoliosis with a Hybrid Bracing Protocol: A Randomized-Controlled Trial

Research Protocol "HBP_V02"
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Abstract

This is a prospective randomized controlled trial investigating the therapeutic effect of the Hybrid Bracing Protocol(HyBP) over the Conventional Brace in enhancing In-brace Correction(IBC) for adolescent idiopathic scoliosis(AIS). Scoliosis is a complex three-dimensional spinal deformity and AIS is the commonest with a high prevalence of 2-4%. If left untreated, AIS can progress resulting in significant health problems including back degeneration and negative body images. Bracing, such as Underarm Brace(UAB) used in our center, is indicated for skeletally immature patients with Cobb angle>20°. Another bracing system is a nighttime Lateral Bending Brace(LBB) designed in a bending position opposite to the convexity of the curve thus resulting in its overcorrection. If AIS becomes severe despite bracing, ultra-major surgery is indicated aiming at bony fusion of the deformed segment with instrumentation. It is therefore important to maximize treatment effectiveness with bracing to control curve progression and to avoid the need for surgery. In-brace Correction(IBC) is the percentage reduction in Cobb angle with bracing. Studies have reported IBC is an important determinant of brace effectiveness. For enhancement of IBC, we put forward the Hybrid Bracing Protocol(HyBP) combining the use of daytime UAB and nighttime LBB. To be best of our knowledge, HyBP has never been reported in the literature. Our pilot study on 8 patients treated with HyBP and 8 Cobb-matched historical controls treated with fulltime UAB showed very promising results with IBC of 42.1±22.0% and 22.1±14.9% in the HyBP and control group respectively. We therefore propose a formal prospective rater-blinded randomized controlled trial on 120 skeletally immature AIS female subjects with single thoracolumbar or lumbar curve newly prescribed with bracing. They are randomly allocated to the HyBP Group or the Conventional Brace Group (CB Group). The primary objective is to determine if the HyBP Group has better treatment effect in terms of In-brace Correction (IBC) when compared with the CB group at 3-month and 18-month after bracing. This is a 3-year study proposal representing the first phase of a project, to be followed by the second phase of the project when all subjects of the entire cohort will be assessed on curve outcome at time of completion of bracing and at 2 years post-bracing. This study will carry significant clinical impacts in that, if proven useful, the HyBP can be used for enhancement of treatment outcomes with bracing, thus preventing the scoliotic spine from deterioration and to avoid the need for surgery.

The objectives of this project are:

1. The primary objective is to determine if the Hybrid Bracing Protocol (HyBP) combining the use of daytime Underarm Brace (UAB) and a nighttime Lateral Bending Brace has better treatment effect in terms of In-brace Correction (IBC) when compared with the conventional fulltime UAB
2. The secondary objectives are :
    a. to determine if the HyBP has better treatment outcomes in terms of control of curve progression when compared with the conventional fulltime UAB for those who have completed bracing treatment or require surgery by the end of this 3-year study proposal
    b. to determine if the HyBP has better outcomes when compared with the conventional fulltime UAB in terms of quality of life as assessed by SRS-22r, Spinal Appearance Questionnaire and the Brace Questionnaire

(a) Background of Research

AIS is a highly prevalent and disabling spinal condition affecting young subjects

Scoliosis is a complex three-dimensional spinal deformity the severity of which is quantitatively assessed with Cobb angle [3]. Scoliosis is a prevalent condition affecting 2- 4 % of the general population [4]. ***Our hospital is one of the two tertiary referral centers for scoliosis in Hong Kong***. Around 800 new referrals are received annually, mainly from School Screening Program of the governmental Student Health Service. As in Oct-2020, 22,434 patients have been managed at our Scoliosis Clinic since its inception in 1987.

Among cases with scoliosis, Adolescent Idiopathic Scoliosis(AIS) is the commonest occupying more than 80% of cases. It commonly occurs in girls between 10-16 years old with a female to male ratio of 7:1 for curves greater than 30 degrees [5]. If left untreated, AIS can progress and be associated with serious health problems including back degeneration, cardiopulmonary compromises, negative body images and psychosocial disorders arising out of grossly deformed torso [1]. Very severe curves can result in early mortality [2].

Treatment for scoliosis: bracing and surgery, and the need to maximize effectiveness of bracing

In general, AIS patients with Cobb angle < 20° are closely monitored at regular intervals. For skeletally immature patients having Cobb angle greater than 20 to 25°, bracing is indicated (Figure 1A).

Bracing can be defined as the application of external corrective forces to the trunk with the goals of halting curve progression in AIS [6]. To achieve this goal, rigid supports or elastic bands can be used. Rigid braces such as the underarm brace used in our Center as depicted in Figure 1A are frequently prescribed in clinical settings. As Wynarsky and Schultz has suggested, apart from the active mechanisms with muscle control to shift the trunk away from the pressure areas, a passive mechanism with 3-point external forces applied by the brace pads could be operating and account for the orthotic control of curve progression in AIS (Figure 1B) [7].

Numerous studies showing therapeutic evidences of bracing have been reported but as a Cochrane review in 2010 has indicated, there was a lack of prospective randomized controlled trial providing Level 1 evidence on brace effectiveness [8]. The situation remained the same until Weinstein et al. conducted the BrAIST study which was a prospective randomized controlled trial on bracing and analyzed both the randomized and preference cohorts and concluded that bracing could be useful in a proportion of cases for controlling curves from progression to the threshold for surgery [9].

As shown by the BrAIST study, some cases do progress even with bracing. Surgery is considered when curves become severe (Cobb angle > 50°) [1, 4]. It is typically in form of spinal fusion resulting in permanent loss of motion of the fused spinal segment. Although surgery can effectively alleviate and stabilize severe curves, it is a major and invasive procedure associated with serious complications including massive blood loss, wound infections, implant failures, spinal cord injuries and even mortality.

In view of the invasive nature of surgical procedures and the significant morbidities with severe scoliosis, it is most important to maximize the effectiveness of bracing treatment for AIS to avoid the need for surgery.

(A) Work done by others investigating impact of initial In-brace Correction (IBC) on treatment effectiveness of bracing

Although bracing is considered to be useful, its effectiveness hinges on various factors

one of which is the in-brace curve correction, ie In-brace Correction (IBC) [12]. IBC is defined as the percentage of Cobb angle reduction during an X-ray with the brace fitted on the patient [10].

In-brace Correction (IBC) = (([Pre-brace Cobb] – [In-brace Cobb])/[Pre-brace Cobb]) x 100%

Yen et al. studied 61 patients and noted the IBC in 48% of patients was less than 15%, 28 % was between 15-30% correction, 16% with 30-50% correction, and 8% had over 50% correction [11]. Xu et al. studied 488 AIS patients and noted failure group (curve progression > 5° at 2-year treatment with bracing) had significantly lower initial IBC and reported the best cut-off of initial IBC was 10% giving an odds ratio of 9.61 [12]. Katz et al. studied 51 AIS patients and reported IBC for double curves of at least 25% significantly increased the likelihood of treatment success [13]. Maruyama et al. followed 33 patients up to skeletal maturity and noted patients in the failure group (progression of Cobb angle of >6°, n=8) had a lower IBC rate (83.4% vs. 37.6% in the failure group) [14]. Bogaart did a recent review showing strong evidence that lack of initial IBC is associated with treatment failure [15]. Karavidas in another systematic review concluded that initial IBC seemed to be the most important predictive factor for successful treatment outcome [10].

In brief, studies have shown that suboptimal IBC is associated with unsatisfactory treatment outcome with bracing. On the other hand, review of the literature indicates majority of reports are observational studies describing the impact of IBC on control of curve progression. While investigations of different bracing designs have been reported aiming at enhancement of IBC and curve control, there remains a lack of randomized interventional study reporting whether combining the use of a daytime rigid brace and a nighttime lateral bending brace can enhance IBC thus leading to better control of curve progression.

(B) Work done by our group on bracing treatment for scoliosis and scoliosis-related randomized controlled trials

Our group has been active in conducting spinal orthotic researches and randomized controlled studies for AIS subjects. Concerning spinal orthotic researches, Co-I Wong conducted a study to compare the CAD/CAM method with the conventional manual method in brace fabrication for AIS and reported the CAD/CAM system could save the time in the rectification process and offer a relatively high resemblance in cast rectification as compared with the conventional manual method [16, 17]. Co-I Wong evaluated the effectiveness of orthotic treatment for AIS using the three-dimensional clinical ultrasound (3D-CUS) by studying 21 patients (3D-CUS group) and 22 patients (control group) and noted 3D-CUS was an effective, non-invasive and fast assessment method for scoliosis, especially useful in enhancing the effectiveness of orthotic treatment [18].

Concerning clinical trials for AIS subjects, PI Lam and Co-I Wong reported the results of a prospective randomized controlled trial on the effect of rigid versus flexible spinal orthosis for AIS both at maturity [19, 20] and at 2 year post-maturity according to the SRS standardized brace studies criteria [21] and noted the treatment outcome with the rigid brace is better than the flexible orthosis. PI Lam carried out a prospective randomized controlled trial on whole body vibration (WBV) therapy for 149 AIS subjects and reported WBV was effective for improving areal bone mineral density at the femoral neck of the dominant side and bone mineral content of the lumbar spine in AIS subjects [22].

(C) Our pilot study showing promising results with the Hybrid Bracing Protocol (HyBP) in enhancing In-brace Correction (IBC)

With strong evidences from previous observational studies that IBC is a key determinant of treatment outcome for bracing [13], it is logical to explore ways of maximizing treatment effectiveness of bracing through enhancement of IBC. As illustrated in Figure 2A, one of our

initial cases had a left thoracolumbar curve progressing from 12° to 20° (Figure 2A). A Lateral Bending Brace (LBB) is applied as shown in Figure 2B. By stretching the concave side of the curve with the LBB, the spinal flexibility is enhanced resulting in an excellent IBC of 80% as shown by the x-ray taken within a daytime Underarm Brace abbreviated as UAB (Figure 2C). With very promising results from these initial cases, a pilot study using historical Cobb-matched controls were conducted. All subjects had either single thoracolumbar or lumbar curve. The treatment group was managed with the Hybrid Bracing Protocol (HyBP) combining the use of conventional UAB during daytime and LBB at nighttime. The controls were historical cases treated with the conventional fulltime UAB. All had IBC measured with the post-brace x-ray taken at 3-month after bracing. The baseline parameters and the IBC are summarized as follows:

	Treatment group with HyBP (Mean ± SD)	Control group (Mean ± SD)	p-value (Mann-Whitney Test)
Number of subjects	8	8	
Curve Type	All had single thoracolumbar or lumbar curve		
Age (years)	13.0 ± 0.8	11.7 ± 0.8	0.012
Risser	3.1 ± 1.0	1.5 ± 1.9	0.072
Cobb angle	25.5 ± 4.7	26.8 ± 5.6	0.560
In-brace Correction	42.1 ± 22.0	22.1 ± 14.9	0.052

This pilot study gave very promising evidences that patients treated with the Hybrid Bracing Protocol did have higher IBC although the difference did not reach statistical significance likely out of Type II error from inadequate sample size.

The gap in knowledge and the need of a randomized controlled trial to test the HyBP

There were limitations with this pilot study. First, it was not a prospective randomized controlled trial. The controls were not contemporary cases but recruited from past consultations. Second, the sample size was small. Third, there was no monitoring of brace compliance and fourthly, there was no long-term follow up with lack of information on final curve severity after skeletal maturity. As mentioned above, there is a lack of study reporting the use of a hybrid bracing protocol for enhancing treatment outcome of bracing through enhancing the in-brace correction. A formal well-designed randomized controlled trial is therefore warranted to fill in this gap in knowledge.

Our hypothesis

We hypothesize that the HyBP has better treatment effect for AIS in terms of IBC and control of curve progression when compared with the conventional fulltime UAB

Our study objectives are:

1. The primary objective is to determine if the Hybrid Bracing Protocol (HyBP) combining the use of daytime Underarm Brace (UAB) and a nighttime Lateral Bending Brace has better treatment effect in terms of In-brace Correction (IBC) when compared with the conventional fulltime UAB
2. The secondary objectives are :
    a. to determine if the HyBP has better treatment outcomes in terms of control of curve progression when compared with the conventional fulltime UAB for those who have completed bracing treatment or require surgery by the end of this 3-year study proposal
    b. to determine if the HyBP has better outcomes when compared with the conventional fulltime UAB in terms of quality of life as assessed by SRS-22r, Spinal Appearance Questionnaire and the Brace Questionnaire

(b) (i)Research plan and methodology

Introduction :- To evaluate the usefulness of the HyBP, we propose a prospective randomized controlled study on 120 skeletally immature female AIS subjects newly prescribed with bracing. They will be randomly allocated to the Conventional Bracing Group (CB Group) or the HyBP Group. Brace treatment for both groups will last till skeletal maturity. Radiographic evaluation of curve severity and logging of brace compliance will be conducted according to standardized protocols at pre-scheduled intervals. Quality of life (QoL) will be assessed with questionnaires validated with local language for the local population. This is a 3-year study proposal representing the first phase of a project, to be followed by the second phase of the project beyond this current proposal when all subjects of the entire cohort will be assessed on curve outcome at time of completion of bracing and at 2 years post-bracing.
The flowchart for this 3-year study proposal is depicted in Figure 3.

Subject Recruitment:- Female subjects newly prescribed with bracing are recruited from our Scoliosis Clinic at Prince of Wales Hospital:

Inclusion criteria:-

1. Females with AIS diagnosed after detailed clinical and radiological evaluation by an experienced orthopaedic surgeon and
2. having a single lumbar or thoracolumbar curve with Cobb angle between 20° - 40° and
3. age 10 years and older when bracing is prescribed and
4. Risser 0 to 2 and
5. either pre-menarchal or less than 1 year post-menarchal and
6. with no prior treatment for scoliosis

Exclusion criteria [9]:-

1. presenting with associated musculoskeletal, neurological or other conditions possibly responsible for the curvature
2. with previous surgical or orthotic treatment or
3. physical or mental disability that prevent patients from complying with the bracing protocol

An initial interview will be conducted with the subject and her legal guardians on details of the aims, the protocol and the timeframe of the study. Questions from the participants will be answered up to their satisfaction. An informed consent will be obtained. Ethical approval will be obtained from CREC (the IRB for our hospital) before the study is implemented. The study will be carried out in compliance with the Declaration of Helsinki and ICH-GCP.

Subject Randomization:- Assignment to a group is by a stratified randomization protocol with a permutated block of 10 to allow recruitment to be spread over 12 months. Allocation concealment is strictly followed to prevent investigators / subjects from knowing or predicting the next allocation. An individual sealed envelope containing the group allocation for the next subject will be open only after the subject agrees to participate and an informed consent is obtained.

The Conventional Bracing Group (CB Group):-

1. *Brace fitting*: The subjects in this group will be treated with the conventional rigid underarm brace (UAB) routinely used in our Center [19, 21] (Figure 1A). A CAD/CAM system (Vorum Research Corporation, Canada) will be used to capture the 3D information of patient's body and to design spinal orthosis through its purpose-design software [16, 17]. The pressure pads are strategically located based on the orthotist's experience in examining the apex of the rib hump and lumbar prominence and information from the software. After

the brace is ready, fine adjustment of location of the pressure pads will be made with reference to an in-brace whole spine radiograph.

2. *Brace compliance monitor*: Each brace will be fitted with a waterproof microsensor brace compliance monitor, the Orthotimer® (dimensions: 9mm x 13mm x 4.5mm and weight <1g), from Rollerwerk-Medical engineering & consulting, Germany. The memory capacities of the brace monitor can last for 400 days. To embed the brace monitor into the brace, a dummy with the same dimensions of the monitor will be placed underneath a soften polyethylene sheet which is used to fabricate a brace. After the polyethylene becomes harden, an empty space for the monitor will be created. No extra attention is needed from the participants. Once the system is turned on, it will log the temperature at the anterolateral waist region. Data from the device will be retrieved during each study visit.

The Hybrid Bracing Protocol Group (HyBP Group):-

1. *Brace fitting*: The subjects in this group will be treated with the conventional rigid underarm brace (UAB) at daytime and a nighttime lateral bending underarm brace, ie the Lateral Bending Brace (LBB) [5,6]. The UAB will be fabricated with the same design as in the CB Group. The nighttime LBB will be fabricated with the 3D information of the patient's body as the conventional rigid underarm brace. The nighttime bending brace will be designed in a bending position opposite to the convexity of the lumbar/thoracolumbar curve. The patient will be positioned to an overcorrection posture inside the nighttime LBB. After the brace is ready, fine adjustment of location of the pressure pads will be made with reference to an in-brace whole spine radiograph. The LBB will further be adjusted until the in-brace radiograph indicates a minimum overcorrection of 10° (Cobb angle = -10°, ie in opposite direction to the original curve)
2. *Brace compliance monitor*: Both the daytime UAB and nighttime LBB will be fitted with the same waterproof microsensor brace compliance monitor as in the CB Group. Data from the device will be retrieved during each study visit.

Other than treatment with different bracing protocols, the same standard orthotic and medical care for treating scoliosis will be provided for both the CB Group and HyBP Group according to the SOSORT "Standards of management of idiopathic scoliosis with corrective braces in everyday clinics and in clinical research" [23]. Subjects are instructed to wear the brace 23 hours daily [6]. The rest hour is for bathing and exercises. Brace compliance in terms of the average number of hours per day of brace wear will be separately evaluated for the daytime UAB and nighttime LBB.

Study Visits, Investigations and Measurements:-

1. *Study visits*: Subjects will be evaluated at baseline just before bracing, 3 months and 6 months after bracing and at 6-monthly intervals thereafter (Figure 3 for details).
2. *Plain radiography of the whole spine in standing position* will be taken with a standard protocol using the EOS system:
    a. Measurements are made as follows
        i. PA view for measurement of:
            a. Frontal Cobb angle of the structural curve [24, 25].
            b. Trunk Shift will be measured in cm indicating the perpendicular distance of mid-point of T1 vertebra from the central sacral line [24],
            c. Curve levels, apex levels, side of curves
        ii. Lateral view for measurement of Cobb angle for thoracic kyphosis and lumbar lordosis

b. Timing
   i. At baseline, 3rd month, 6th month, then every 6 months thereafter
      a. PA and lateral x-ray are taken without brace for monitoring of curve severity
   ii. At 3rd month, and 18th month
      a. PA and lateral x-ray is taken without brace, then followed by taken with the daytime UAB for evaluation of In-brace Correction
   iii. (At completion of brace fitting, a supine AP x-ray of whole spine taken with LBB will be assessed with the frontal Cobb angle)
c. In-brace Correction (IBC) = (([Pre-brace Cobb] – [In-brace Cobb])/Pre-brace Cobb) x 100% . It will be evaluated at the 3-month and 18-month time-points
d. ***Radiographic measurements will be done by a single experienced rater who is blinded to subject's grouping (he will not be shown the x-ray taken with the LBB)***.

3. *Brace compliance monitoring* :- data on brace usage from the aforementioned monitoring devices will be retrieved at each study visit. The body temperature collected from the sensor will be used for compliance analysis and 32° Celsius is set as the compliance threshold [26].
4. *Quality of Life (QoL) Questionnaires* :-
   This will be conducted according to the standard protocol at baseline and the 18-month time-point for self-administration of the following:
   a. SRS-22r [27]
   b. Spinal Appearance Questionnaire (SAQ) [28]
   c. Brace Questionnaire (BrQ) [29]
   The Chinese versions for SRS-22r, SAQ and BrQ have all been validated and ready for use in this study [30-33].
5. *Anthropometric and maturity assessment*:-
   Body weight, standing height, sitting height and arm span will be measured at each study visit according to the standard protocol. The "menarchal year", defined in a way similar to that by Lehtonen-Veromaa et al [34], is the age at menarche subtracted from the current age (i.e., [current age – age of menarche] in years). For pre-menarchal subjects, the age of menarche is determined at subsequent study visits.

End of Brace Treatment :-
Brace treatment will be stopped with one of the following conditions:

1. At skeletal maturity: bracing will be stopped at maturity following a standardized protocol of weaning. Maturity is defined as [35]:
   a. Risser sign 4 or more and
   b. with no change in height or <1 cm change in standing height over 2 consecutive visits 6 months apart and
   c. 24 months post-menarchal
2. When surgery for scoliosis is done. The indication for surgery in our center is Cobb angle > 55° despite treatment with braces.
3. If subjects decline further treatment with bracing of their own accord

Post-brace curve outcome and treatment success:- Apart from the primary objective of assessing IBC, effectiveness of bracing treatment will also be assessed with respect to post-brace curve outcome, ie curve severity after cessation of bracing treatment as follows:

1. Increase in Cobb angle ≤ 5° for the structural curves at skeletal maturity
2. Cobb angle remains ≤ 45° at skeletal maturity
3. Cobb angle remains less than surgical threshold of 55° at skeletal maturity

Maintenance of Compliance :- Compliance with treatment protocol will be emphasized from time to time. To aim at a high level of compliance for both groups, we will explain to the patients and their legal guardians in details about the purposes of the study. Rapport is emphasized. Our RA will make regular phone contacts with the subjects of both groups to provide support and enquire about their situation, indicate concerns about their difficulties, answer any queries and remind them of the importance of adherence to the treatment protocol. We will also engage active participation of the parents. With experiences from previous clinical trials involving adolescent scoliosis subjects [22], we are confident that subjects will be compliant with the study protocol.

Persistence of study in COVID-19 pandemic environment:-
Research investigations are done during routine clinic visits. Since AIS subjects will need to come back for follow-up of their scoliosis even during a pandemic, this study will persist and not be affected even under the COVID-19 or other infection disease pandemic environment.

Statistical Analysis:-
The spread of data will be tested for normality. For data that is normally distributed, the numerical data are expressed as mean ± SD. Otherwise they are expressed as median (interquartile range). Demographic data, anthropometric data, QoL scores, initial Cobb angle and other curve morphological data between the two groups at baseline will be compared using two-sided independent student's t-test or Chi-square test as appropriate.
To analyze treatment outcomes, the "Intention-to-Treat" approach is adopted. For the primary objective, two-sided independent student's t-test will be used to compare between-group IBC. For secondary objectives, Chi-square test will be used for comparing the proportions of successful treatment between the two groups. Logistic regression and linear regression model will be used for control of confounding from brace compliance and variables that are unbalanced at baseline between the study groups. QoL scores at the 18-month time-point for the two study groups will be compared with ANCOVA for adjustment of effect from baseline QoL scores. A p value of < 0.05 is considered statistically significant. SPSS 20.0 for Windows will be used for statistical analysis.

Sample size estimation:-
No similar study of this nature has been reported in the literature. According to our pilot study, the effect size is 1.065. Given the limitations with the pilot study as mentioned above, a more conservative and lower effect size of 0.8 will be adopted for sample size estimation. Assuming an alpha value of 0.025 and a statistical power of 0.95, 49 subjects are required for each group. Assuming a dropout rate of approximately 20% for each group, a total sample size of 120 subjects with 60 subjects in each group are required.

Figure 1A: The rigid underarm brace (Conventional Brace) used in this study

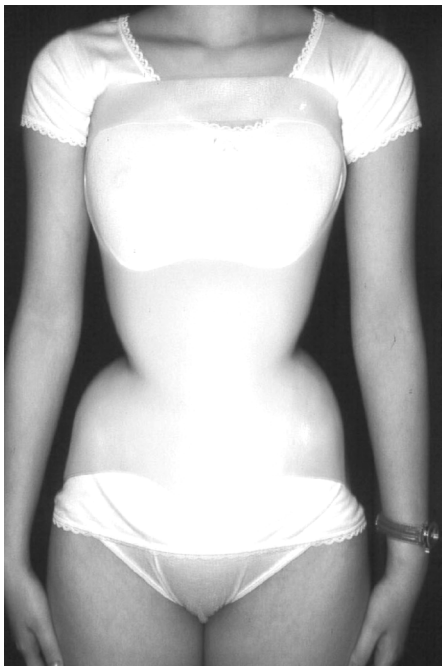
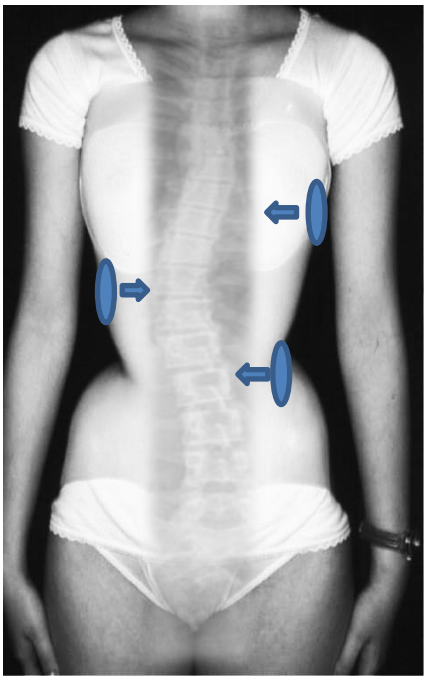


Figure 1B: Key pressure areas with paddings and the 3-point control system



In-brace Correction (IBC) with the Hybrid Bracing Protocol (HyBP)

Figure 2A: Before bracing

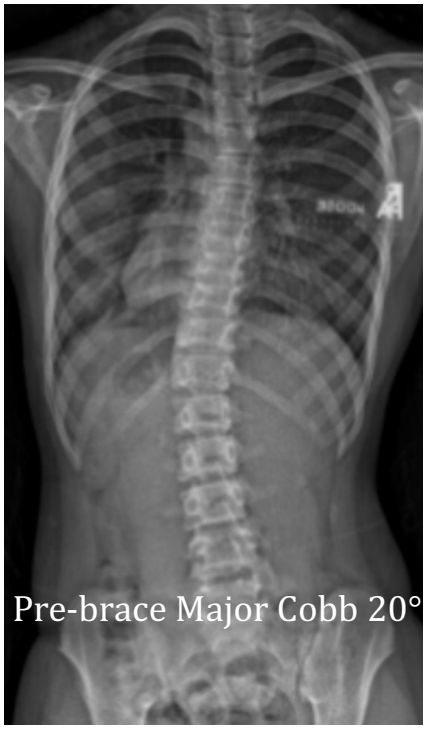


Figure 2B: x-ray taken with Lateral Bending Brace (LBB)

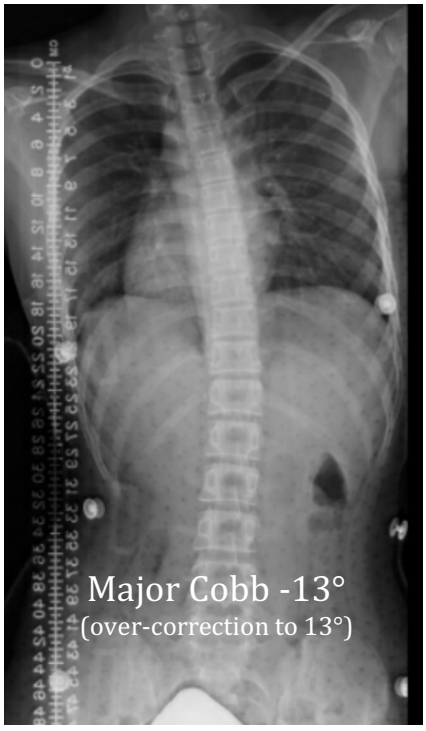


Figure 2C: x-ray taken with Underarm Brace (UAB)

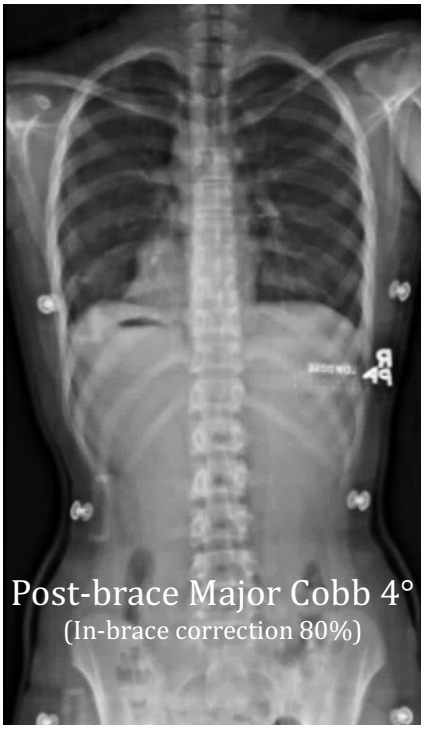
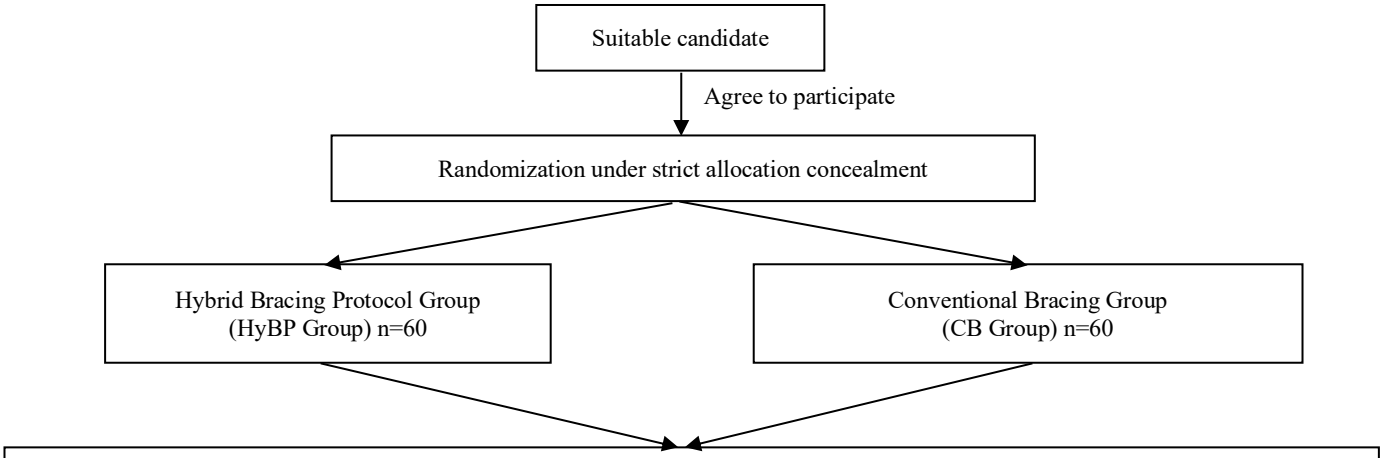


Figure 3: Study flowchart



1. Study visit
   a. Baseline (just before bracing), 3rd month, 6th month, then every 6 months thereafter
2. Investigations at each study visit
   a. radiographic evaluation
      i. Measurements:
         - PA view
            i. Cobb angle of structural curves
            ii. Trunk Shift, curve levels, apex levels, side of curves
         - Lateral view
            i. Cobb angle for thoracic kyphosis and lumbar lordosis
      ii. Timing:
         - At baseline, 3rd month, 6th month, then every 6 months thereafter
            i. x-ray is taken without brace for monitoring of curve severity
         - At 3rd month, and 18th month
            i. x-ray is taken without brace, then followed by taken with the daytime UAB for evaluation of IBC
         - At completion of brace fitting, the supine AP x-ray of whole spine taken with LBB will be assessed with the frontal Cobb angle
   b. Logging of brace compliance
   c. QoL questionnaires: SRS-22r, SAQ and BrQ at baseline and the 18-month time-point
   d. Anthropometric measurements: body weight, standing height, sitting height, arm span
   e. Maturity assessment: age, "menarchal year", Risser sign

End of brace treatment at (i) skeletal maturity or (ii) when surgery is done or (iii) when subjects decline further bracing

A. Within the 3-year study period of this current GRF proposal
   1. Primary objective is to compare between the HyBP Group and CB Group regarding
      a. in-brace correction at 3rd month and 18th month of bracing
   2. Secondary objectives are to compare between the HyBP Group and CB Group for the following:
      a. For subjects who have completed bracing treatment or require surgery by the end of this 3-year study period, curve outcome will be assessed according to:
         1. Percentage with increase in Cobb angle ≤ 5° for the structural curve at skeletal maturity
         2. Percentage with Cobb angle remains ≤ 45° at skeletal maturity
         3. Percentage with Cobb angle remains less than surgical threshold of 55° at skeletal maturity
      b. QoL status at baseline and their changes at 18th month of bracing

B. Beyond the 3-year study period of this current GRF proposal into the second phase of the entire project, evaluation for the entire cohort will be performed at completion of bracing treatment, and at 2-year after cessation of bracing for:
   1. Evaluation of curve outcome according to:
      1. Percentage with increase in Cobb angle ≤ 5° for the structural curve at skeletal maturity
      2. Percentage with Cobb angle remains ≤ 45° at skeletal maturity
      3. Percentage with Cobb angle remains less than surgical threshold of 55° at skeletal maturity
   2. QoL status

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