Design:

This study is a prospective and single blinded randomized control trial. The inclusion or the exclusion criteria will be assessed by the same physician before the patients are invited to join the trial. After the selected patients have signed the informed consent sheets, they will be randomized into two groups (21 patients in each group), the radial shockwave therapy group (RSWT group), the botulinum toxin injection group, and the control group. The randomization will be generated by a computer program and the allocation will be done with concealed envelops. Both the patients and the examining physicians are blind to the allocation. Treatment will be performed by another independent physician.

Participants:

Totally, 42 patients will be recruited from the department of Physical Medicine and Rehabilitation of the Taipei MacKay Memorial Hospital. Eligible subjects should meet the following inclusion criteria: (1) aged between 18 ~ 80 years old; (2) at least 6 months since onset of last stroke; (3) having at least 1+ in modified Ashworth Scale (MAS) score at the spastic elbow; (4) most important of all, read and signed the inform concern of this study.

The exclusion criteria are the following: (1) patients with elbow contracture (MAS=4); (2) patient who had prior history of botulinum toxin, phenol, alcohol injections, intrathecal baclofen pump or rhizotomy in six months; (3) having evidence of cognitive deficit; (4) having local infection, severe inflammation or otherwise lesion that is not suggestive for ESWT; (5) patient with serious medical problems, as uncontrolled hypertension,

coagulopathy, recent severe hemorrhage, neoplasm, severe hepatic disease, epilepsy, cutaneous pathology, mental retardation.

During the study period, physical therapy including range of motion (ROM) exercises, stretching, and others remained unchanged. Also, the doses of medication which might affect spasticity were not changed.

Interventions:

For each group, totally 3 section of therapy will be given in an interval of one week. The shock wave will be given by a two combined ESWT device from which 3000 impulses of shock waves with energy flux density of 1.5 bars and frequency of 5 Hz are delivered in the radial shock wave therapy group. For botulinum toxin group, botulinum toxin (dilution 500 U/2 mL in saline 0.9%) was administered. For the control group, a sham probe will be contacting the skin with the same therapeutic sound made. However, no energy will be delivered from the sham probe. The location of the applied therapy will be at biceps, flexor carpi radialis (FCR) and flexor carpi ulnaris (FCU) muscles**.**

Outcome measures:

The primary outcome of this study include, elbow andradio carpal joint range of motion (ROM), modified Ashworth scale (MAS), modified Tardieu scale (MTS), and Fugl-meyer assessment (FMA). The evaluation will be done before therapy sections, immediately, 1 month after, and 3 months after 3rd section of therapy. All examination will be done by the same examining physician who is blind to the allocation.

Modified Ashworth scale (MAS). The definition of the measured scales were as that proposed by Bohannon and Smith.[3] Briefly, elbow joint range of motion will be performed manually. MAS is graded by the resistance felt during passive range of motion. However, for convenience in the statistical analysis, MAS 1+ was substituted by scale of 2, and 2, 3, and 4 were substituted by 3, 4, and 5, respectively.

Modified Tardieu scale (MTS). The definition of the measurement was as that proposed by Boyd and Graham (modified from Tardieu scale).[4 5] In brief, the measurement of elbow and radio carpal range of motion will be performed at a slow and a fast velocity. The resulted joint angles at two speeds will be measured by goniometer. R1 angle is defined as angle of catch after a fast speed stretch and R2 angle is defined as angle measured during slow speed range of motion. The average of three testing will be used for analysis. The quality of muscle reaction during measurement will also be scaled.

Fugl-meyer assessment (FMA) The Fugl-Meyer assessment is designed to assess motor recovery following stroke. The maximum score of motor function of upper limbs were 66. It is a relatively simple assessment to administer and requires minimal training. The overall reliability for this instrument was high, as were the reliability measurements for the subsections of this assessment.

Statistical analysis.

All statistic data will be analyzed by SPSS statistical software, version 20.0 (SPSS Inc., Chicago, USA). The homogeneity of patient demographic

characteristics in both comparative groups A and B were calculated with chi-square test for qualitative variables (gender, stroke subtype, affected site) and the ANOVA test for quantitative variables (age, weight,height, body mass index [BMI], time since onset of stroke). The differences between 3 groups were investigated using the repeated measures ANOVA followed by the Bonferroni post hoc tests. Statistical significance was set at $P<0.05$.