

行政院國家科學委員會專題研究計畫 成果報告

以直腸超音波引導注射肉毒桿菌毒素於尿道外括約肌來治
療逼尿肌尿道外括約肌失調之療效
研究成果報告(精簡版)

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計畫主持人：黃玉慧
共同主持人：陳順郎、畢柳鶯

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行政院國家科學委員會補助專題研究計畫 成果報告
 期中進度報告

計畫名稱：以直腸超音波引導注射肉毒桿菌毒素來治療逼尿肌尿道外括約肌失調之療效

The effect of transrectal ultrasound-guided botulinum toxin injection to external urethral sphincter in treating detrusor external sphincter dyssynergia

計畫類別： 個別型計畫 整合型計畫

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執行單位：中山醫學大學

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中文摘要

研究目的：評估以直腸超音波引導注射肉毒桿菌毒素於尿道外括約肌，以治療脊髓損傷病患併有逼尿肌尿道外括約肌失調之療效 (detrusor external sphincter dyssynergia, DESD)。

研究對象：18 個脊髓損傷病患併有逼尿肌尿道外括約肌失調患者。

研究方法：在直腸超音波引導下，找到位於攝護腺外方的尿道外括約肌，在會陰部直接注射 100 單位的肉毒桿菌毒素 (稀釋在 2 毫升的生理食鹽水)。注射前及注射後一個月，安排尿動力學檢查，並記錄病患之殘尿量，追蹤達六個月。統計分析方法：以 paired t-test 檢定治療前後的最大逼尿肌壓力、漏尿時膀胱內壓、尿道壓力、整合式肌電圖、及殘尿量變化，是否有統計上的差異 ($P < 0.05$)。

研究結果：尿動力學檢查結果方面，在整合式肌電圖及尿道壓力均有明顯變化 ($P < 0.05$)，但在最大逼尿肌壓力及漏尿時膀胱內壓並沒有明顯變化。病患的殘尿量有明顯改善，尤其在注射後的一個月及兩個月 ($p < .012$)。

結論：直腸超音波引導下，於會陰部直接注射肉毒桿菌毒素，可以有效減少病患的殘尿量。因為此方法不需要以膀胱內視鏡來進行，故可以由一般復健科醫師來執行，是方便有效的方法。

英文摘要

Objective: To evaluate the effects of a single, trans-rectal, ultrasound-guided (TRUS-guided) trans-perineal injection of botulinum toxin A (BoNT/A) to the external urethral sphincter (EUS) for treating detrusor external sphincter dyssynergia (DESD).

Design: Descriptive study.

Setting: Rehabilitation hospital affiliated with a medical university.

Participants: Patients (N=18) with supra-sacral spinal cord injury who had DESD confirmed on video-urodynamic study.

Interventions: A single dose of 100 units BoNT/A was applied into the external urethral sphincter via trans-rectal ultrasound-guided trans-perineal route injection.

Main Outcome Measures: Maximal detrusor pressure, detrusor leak-point pressure, integrated electromyography, maximal pressure on static urethral pressure profilometry and post-voiding residuals.

Results: There were significant reductions in integrated electromyography (EMG) ($p = .008$) and static ($p = .012$) and dynamic urethral pressure ($p = .023$), but not in detrusor pressure and detrusor leak-point pressure after treatment. Post-voiding residuals also significantly decreased in the 1st and 2nd month after treatment ($p < .012$).

Conclusions: TRUS-guided trans-perineal injection of BoNT/A has beneficial effects in treating DESD.

關鍵詞

關鍵字：超音波，肉毒桿菌毒素，膀胱，尿動力學

Key words: *ultrasonography, botulinum toxins, urinary bladder, urodynamics,*

報告內容

Title:

Transrectal Ultrasound Guided Transperineal Botulinum Toxin A Injection to the External Urethral Sphincter for Treatment of Detrusor External Sphincter Dyssynergia in Patients with Spinal Cord Injury

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Running head:

TRUS guided botulinum toxin injection in treating DESD

1 **Title: Transrectal Ultrasound Guided Transperineal Botulinum Toxin A Injection**
2 **to the External Urethral Sphincter for Treatment of Detrusor External Sphincter**
3 **Dyssynergia in Patients with Spinal Cord Injury**

4

5

ABSTRACT

6 **Objective:** To evaluate the effects of a single, trans-rectal, ultrasound-guided
7 (TRUS-guided) trans-perineal injection of botulinum toxin A (BoNT/A) to the external
8 urethral sphincter (EUS) for treating detrusor external sphincter dyssynergia (DESD).

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14 sphincter via trans-rectal ultrasound-guided trans-perineal route injection.

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16 integrated electromyography, maximal pressure on static urethral pressure profilometry
17 and post-voiding residuals.

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19 $=.008$) and static ($p=.012$) and dynamic urethral pressure ($p=.023$), but not in detrusor
20 pressure and detrusor leak-point pressure after treatment. Post-voiding residuals also

1 significantly decreased in the 1st and 2nd month after treatment ($p<.012$).

2 **Conclusions:** TRUS-guided trans-perineal injection of BoNT/A has beneficial effects in
3 treating DESD.

4 **Key words:** *ultrasonography, botulinum toxins, urinary bladder, urodynamics,*
5 *autonomic dysreflexia*

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List of Abbreviations

| | |
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| TRUS | transrectal ultrasound |
| EUS | external urethral sphincter |
| BoNT/A | botulinum toxin A |
| DESD | detrusor external sphincter dyssynergia |
| DISD | detrusor internal sphincter dyssynergia |
| EMG | electromyography |
| SCI | spinal cord injury |
| PVR | post-voiding residuals |
| IEMG | integrated electromyography |

1 **Title: Transrectal Ultrasound Guided Transperineal Botulinum Toxin A Injection**
2 **to the External Urethral Sphincter for Treatment of Detrusor External Sphincter**
3 **Dyssynergia in Patients with Spinal Cord Injury**

4

5 Detrusor sphincter dyssynergia is inappropriate contraction or failure of relaxation of
6 either internal (DISD) or external (DESD) urethral sphincter during detrusor contraction.¹

7 It affects 96% of supra-sacral spinal cord injury (SCI) cases.² DISD is encountered less
8 often in this group patients. DESD causes urinary retention, recurrent urinary tract
9 infection, autonomic dysreflexia, high intra-vesicle pressure, vesico-ureteral reflux, and
10 renal damage, and remains the main cause of morbidity and mortality in SCI patients.³⁻⁵

11 Different therapeutic strategies, including oral medication and surgery, have been
12 proposed but these are usually ineffective or have side effects.⁶⁻⁹

13 Botulinum toxin A (BoNT/A) inhibits acetylcholine release at the neuromuscular
14 junction, thereby decreasing muscle contractility for 3-6 months.¹⁰ It is successfully used
15 in treating focal dystonia and spasticity of skeletal muscles of the face, neck, pharynx,
16 and limbs.¹¹⁻¹⁴ Thus, BoNT/A injections into the external urethral sphincter represent a
17 valuable alternative to surgical sphincterotomy.¹⁵ It has been first reported as a treatment
18 for DESD by Dykstra et al. in 11 SCI patients, with reduction of urethral pressure and
19 post-voiding residuals (PVR).¹⁶ Schurch et al., among others, also reported the effect of
20 BoNT/A, injected either trans-urethral via cystoscopy or trans-perineal with

1 electromyography (EMG).^{15, 18-24}

2 The trans-perineal technique is preferred to the cystoscopic approach, which is more
3 invasive and often requires spinal or general anesthesia.²⁵ However, the exact placement
4 of the injection needle is important not only to achieve the desired therapeutic goals but
5 also to minimize waste of BoNT/A. Despite well-described EMG guided methods, EMG
6 of the external urethral sphincter is difficult. It is also impossible to definitively exclude
7 false recording of the surrounding perineal musculature.²⁵ Trans-rectal ultrasound (TRUS)
8 is an effective method to visualize the lower urinary tract. Its use is rapidly becoming part
9 of routine urologic investigations in patients with prostatic disease. Using a multi-plane
10 endosonoprobe, urethral and para-urethral structures are scanned either sagittally or
11 transversely at any level.²⁶

12 In order to more accurately localize the BoNT/A injection site in the external
13 urethral sphincter, and facilitate needle placement, a new method has been designed using
14 TRUS guidance. This is a report on the results of a preliminary study investigating the
15 feasibility of TRUS-guided trans-perineal injection of 100 units BoNT/A to the external
16 urethral sphincter of SCI patients with DESD.

17

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METHODS

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1 **Participants**

2 The study subjects were male patients aged > 18 years with supra-sacral SCI from
3 the rehabilitation department ward. The inclusion criterion was the presence of DESD,
4 which was defined as inappropriate contractions of the external urethral sphincter with
5 concomitant detrusor contractions documented by urodynamic studies like
6 needle-electrode EMG and voiding cysto-urethrometrography. All of the patients were
7 neurologically stable (i.e. no progression of the neurologic symptoms in the previous 3
8 months) but suffered from post-voiding urine volume >150 ml that was unresponsive to
9 oral spasmolytic agents (i.e., hyoscine butylbromide), skeletal muscle relaxants (i.e.,
10 baclofen), and alpha-blockers (i.e., doxazosin mesylate and terazosin).

11 Woman was excluded from the enrollment because the prostate gland was an
12 important landmark of TRUS. Detrusor internal sphincter dyssynergia (DISD) was
13 likewise excluded by evaluation of the bladder neck opening during cystography on
14 video-urodynamic examination. The exclusion criteria also included coagulopathy
15 disease, myasthenia gravis, aminoglycoside treatment, hypersensitivity to BoNT/A, other
16 causes of outlet obstruction (i.e. urethral stricture or benign prostate hyperplasia),
17 previous sphincterotomy, and BoNT/A injection to the external urethral sphincter.

18 The Ethics Committee of Chung Shan Medical University Hospital approved the
19 study. Each patient provided written informed consent. All treatment procedures were on

1 an outpatient basis. All enrolled patients must discontinue alpha blocker, spasmolytic
2 agents and antimuscarinic agents one week before toxin injection. No alpha blocker,
3 spasmolytic agents or antimuscarinic agents are prescribed in the follow-up period.

4 Eighteen patients were enrolled from September 2006 to January 2008. Their basic
5 demographic data were shown in table 1. Their mean age was 36.7 ± 13.3 years (range
6 18-55 years), and their distribution of spinal cord injury (SCI) levels was 13 (72%)
7 cervical and five (28%) thoracic. The average period between the onset of spinal cord
8 injury and inclusion was 14.9 ± 12.3 months (range 4-47 months). Using the International
9 Standards of the Neurological and Functional Classification of Spinal Injuries, commonly
10 known as the American Spinal Injury Association (ASIA) scale, 9 (50%) were Grade A, 5
11 (27.8%) Grade B, 3 (16.7%) Grade C, and 1 (5.5%) Grade D.

12

13 **Procedures**

14 With the patient on a left lateral position, a BK type 8808 ultrasound scanner with
15 trans-rectal 7.5 MHz three-dimensional multi-planar transducer probe^a was used as
16 routine trans-rectal ultrasonography. Scanning was initiated from the apex of the prostate
17 gland with the transverse and horizontal planes. The scanning plane was changed to the
18 longitudinal mode when a relatively hypo-echoic external urethral sphincter was
19 identified.

1 The 100 units BoNT/A (Botox) was diluted with 2ml 0.9% saline and inserted into
2 the perineum via 12-cm, 25-gauge spinal needle. The location and depth of injection
3 needle was determined freehand with by TRUS guidance (fig 1A). The needle was
4 inserted further until it reached the level of external urethral sphincter, which was more
5 clearly demonstrated on the ultrasound monitor by pinching the patient's glans penis to
6 induce bulbocavernous reflex (fig 1B).

7 The prepared BoNT/A was injected with continuous sonographic monitoring after
8 confirming the location of the needle tip. An additional 0.2 ml normal saline was then
9 injected to ensure that the maximum amount of toxin in the needle was delivered. Blood
10 pressure was monitored during the whole procedure and any adverse events related to the
11 injection were recorded.

12 Video-urodynamic study, performed with Urodyn 5500 apparatus^b was obtained
13 from each subject before and 4 weeks after the BoNT/A injection. This examination
14 included filling cysto-urethrometrography, sphincter EMG, and static urethral pressure
15 profilometry. Cysto-urethrometrography was done via a triple lumen catheter that
16 measured intra-vesical and urethral pressures synchronously with continuous filling of
17 isotonic saline at a rate of 30ml/min. The measuring point of urethral pressure was at the
18 level of maximal urethral pressure.²⁷

19 Trans-perineal EMG of the external urethral sphincter was obtained via disposable

1 concentric needle electrodes. The needle was inserted into the perineum midline about
2 1.5-2 cm anterior to the anus. A gloved finger in the rectum monitored the position of the
3 prostate while the electrode was directed towards its apex. Electromyographic monitoring
4 of motor unit activity and fluoroscopic examination of the needle position determined the
5 final localization.²⁸

6

7 **Clinical Outcome Measures**

8 Integrated EMG was obtained at a rate of 30Hz while an average of 30-second
9 durations around the maximal value were used for comparison.²⁴ Urethral pressure
10 profilometry was performed with a filling rate of 4 ml/min and catheter withdrawal rate
11 of 1 mm/min. All descriptions and terminologies were according to the recommendations
12 of the International Continence Society. Maximal detrusor pressure, maximal urethral
13 pressure, and maximal detrusor leak point pressure on cysto-urethrometrography, mean
14 integrated EMG (IEMG) of the external urethral sphincter, and maximal urethral pressure
15 on urethral pressure profilometry were used for comparison.

16 The PVR was measured by catheterization pre- and post-injection on the 1st, 2nd,
17 3rd, and 6th months. Patients without spontaneous voiding or those relieved by clean
18 intermittent self-catheterization or indwelling catheters were defined as PVR of 500 ml.
19 The frequency and intensity of autonomic dysreflexia were also recorded.

1

2 **Data Analysis**

3 Wilcoxon signed-ranks test compared urodynamic parameters pre- and post-BoNT/A
4 injection. Friedman test was used to analyze longitudinal data (PVR) and Wilcoxon
5 signed-ranks test with Bonferroni correction was used for *post-hoc* analysis. The level of
6 significance for all tests was at $p < .05$.

7

8

RESULTS

9 The video-urodynamic study, performed at an average of 33.3 days post-injection,
10 revealed significant reduction in dynamic urethral pressure, IEMG, and static urethral
11 pressure compared to pre-injection values (mean reduction percentages \pm standard
12 deviation were 20.4 ± 21.0 , 41.0 ± 44.3 , and 21.6 ± 23.1 , respectively; $p < .05$). There was no
13 significant maximal detrusor pressure decrease after BoNT/A injection ($p = .054$). Fifteen
14 patients with urine leakage in the first video-urodynamic study did not show significantly
15 decreased detrusor leak point pressure after treatment (mean reduction percentage
16 5.5 ± 11.7 ; $p = .376$). All measurements from the video-urodynamic study were presented in
17 table 2.

18 Two patients had clean intermittent self-catheterization for bladder emptying so their
19 PVRs were measured as 500 ml. PVR decreased in the 1st, 2nd, 3rd, and 6th month

1 post-treatment (mean reduction percentages were 37.1 ± 28.13 , 34.0 ± 30.81 , 30.56 ± 35.78 ,
2 and 23.06 ± 31.35 , respectively; $p<.05$). There was significant decrease only in the 1st and
3 2nd months post-treatment after Bonferroni correction of the p value due to multiple
4 comparisons ($p<.012$). All PVR changes were summarized in table 3.

5 Five patients with pre-treatment autonomic dysreflexia had decreased frequency and
6 intensity (blood pressure elevation). There were no serious side effects related to BoNT/A
7 injection and only 1 patient presented with mild hematuria for 1 day.

8

9

DISCUSSION

10 This is the first study to demonstrate the effect of TRUS-guided trans-perineal
11 BoNT/A injection into the external urethral sphincter for treating DESD. The results
12 show that BoNT/A injections via TRUS-guided trans-perineal route can significantly
13 reduce the static and dynamic urethral pressures similar to those in previous reports of
14 transurethral injection.^{15-20, 24} This improvement in voiding function eradicates or lessens
15 the common consequences of urinary retention in SCI patients, such as discomfort while
16 attempting to void urine, autonomic dysreflexia and repeated urinary tract infection.

17 Although the results show a significant reduction of urethral pressure, it is still an
18 indirect way of determining the effects of BoNT/A. Instability while measuring pressure
19 also seems to be a problem. There can be variations up to 50% of the measured value can

1 be seen with different orientations of the catheter.²⁹ Static urethral pressure profile also
2 has time variations that hinder reproducibility and comparability of this measurement.²⁸
3 Reliable and reproducible urodynamic parameters are still needed to evaluate treatment
4 effects. Traditionally, reduced EMG activity is reported by just observing the appearance
5 of raw EMG.^{17, 21, 22} Direct measurements of external urethral sphincter activity by EMG
6 may be a more convincing way to evaluate the net effect of BoNT/A. The original EMG
7 waveform is a cluster of motor unit action potentials, which have upward and downward
8 deflections due to the propagating muscle action potentials, and is hard to directly
9 quantify. The integral of a waveform increases in proportion to the amplitude, frequency,
10 and duration of the original potential, usually relating linearly to the isometric tension up
11 to the maximal contraction. Integrated EMG can quantify changes and validate the
12 effectiveness of BoNT/A treatment.²⁴ It is a relatively objective parameter for evaluation
13 of BoNT/A effect.

14 Both trans-urethral and trans-perineal injections are efficient in suppressing or
15 ameliorating DESD. The trans-perineal approach is easier to perform for a physiatrist
16 who takes care of SCI patients but not trained to perform cystoscopy. It does not require a
17 post-injection in-dwelling Foley catheter and prophylactic antibiotics for cystoscopy. SCI
18 patients with DESD can undergo this procedure at an outpatient facility without
19 anesthesia or antibiotics.¹⁸ In previous reports on trans-perineal injection, complementary

1 targeting technology with EMG guidance is necessary to secure localization of the
2 external urethral sphincter.^{25,28} However, it is debatable whether EMG recordings truly
3 disclose the activity of the external urethral sphincter and not of the surrounding perineal
4 musculature, which will make the effect of treatment doubtful.²⁵

5 Trans-rectal ultrasound is an effective tool to visualize the lower urinary tract. This
6 uncomplicated procedure also allows for an exact assessment of all parts of the external
7 urethral sphincter.³⁰ Aside from providing anatomical details, the development of
8 multi-planar high-resolution probes allows for the accurate targeting of specific injection
9 areas, if required. Visualization of the regional anatomy on the ultrasound monitor is an
10 additional benefit in minimizing the possibility of injecting BoNT/A injection elsewhere
11 because it facilitates the targeting of the external urethral sphincter.³¹ On the monitor,
12 identifying the external urethral sphincter is facilitated by asking study subjects to
13 simulate arresting micturition or to contract voluntarily the pelvic floor muscles.³² These
14 maneuvers are difficult for SCI patients. Instead, pinching the glans penis induces the
15 bulbocavernous reflex to effect a similarly clear visualization of the external urethral
16 sphincter during BoNT/A injection. Thus, the precise injection location is also obtained.

17 Unlike quadrant injections by cystoscopy, asymmetric external urethral sphincter
18 localization of BoNT/A by trans-perineal route can be questioned. The premise is that
19 BoNT/A diffuses all around the external urethral sphincter or that partial weakening of

1 the external urethral sphincter is sufficient to ameliorate DESD.²⁵ The benefits provided
2 by BoNT/A are clear both in the clinical findings such as voiding facilitation, lowering of
3 PVR and attenuation of autonomic dysreflexia as well as urodynamic study such as
4 urethral pressure and IEMG. It shows an ongoing improvement of voiding function in
5 PVR, IEMG, dynamic urethral pressure and static urethral pressure despite insignificant
6 changes in detrusor leak point pressure and maximal detrusor pressure. Possible
7 explanations may be culled from two previous studies. Cote et al.³³ reported in 1981 that
8 long-term bladder outlet obstruction by benign prostate hyperplasia is often associated
9 with detrusor hyper-reflexia that can persist up to 3 months after resolution of the
10 obstruction. De Seze et al. also proposed that after BoNT/A injection to SCI patients with
11 DESD, detrusor leak point pressure decreases later than the maximal urethral pressure.¹⁹
12 In the current study, some patients with strong and continuous DESD initially may have
13 intermittent sphincter activity after this BoNT/A injection (fig 2). These may also partly
14 explain why detrusor leak point pressure and maximal detrusor pressure are not improved
15 as much as IEMG and urethral pressure. In addition, the change from continuous and
16 severe DESD to intermittent and less prominent pattern would lead to shorten the interval
17 of high-pressure voiding (we did not measure this in this study). If it is the case, the risk
18 of upper urinary tract damage caused by high voiding pressure may be reduced.

19 Although, IEMG also significantly decreases after BoNT/A treatment in this report,

1 it may be due to the similar locations of trans-perineal EMG needle recording and TRUS-
2 guided BoNT/A injection. There is no sufficient evidence to prove that either BoNT/A
3 diffuses all around the external urethral sphincter or that partial weakening of the external
4 urethral sphincter contributes to the improvement of DESD.

5 DISD is independent of DESD and may be one of the reasons why some patients do
6 not have improved PVR after urethral sphincter BoNT/A injection.¹⁵ This study excludes
7 DISD by evaluating bladder neck opening on contrast cystography. The mean PVR
8 decreases from 292 ml to 178 ml with a mean reduction percentage of 37.1 in the 1st
9 month post-injection. The toxin effects decrease gradually but PVR improvement persists
10 until the 6th month, even though statistical significance is only noted in the 1st and 2nd
11 months after Bonferroni correction for multiple comparisons.

12 Although this study confirms the effect of a single TRUS-guided trans-perineal
13 injection of 100 units BoNT/A in selected SCI patients with DESD, there are still some
14 limitations. First, there are only eighteen male patients, which is insufficient as conclusive
15 proof. Larger, prospective, controlled studies are still required to establish the overall
16 effectiveness of the proposed method. Second, TRUS-guided trans-perineal injection
17 method needs the prostate gland as an important anatomic landmark. Even though men
18 account for 80% of SCI patients³⁴, the usefulness of TRUS-guided trans-perineal
19 BoNT/A injection may be limited in women who suffer from SCI with DESD. Third,

1 TRUS training is easier for physicians who are not skilled in cystoscopy, acquiring
2 expertise in TRUS still involves some learning curve. Fourth, video-urodynamic study
3 is conducted only in the first month and there is no significant drop of detrusor pressure
4 after relief of outlet obstruction by BoNT/A injection at this early stage. In future studies,
5 long-term follow-up of video-urodynamic study will demonstrate more clearly the
6 response of detrusor pressure to BoNT/A injection.

7

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CONCLUSIONS

9 This study demonstrates the effect of a single TRUS-guided trans-perineal injection
10 of 100 units BoNT/A for DESD in SCI patients without DISD. It provides an alternative
11 treatment option for physicians who care for SCI patients with DESD but who are not
12 trained to perform cystoscopy.

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Suppliers

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- b. Medtronic Urology, Dantec Medical A/S. Tonsbakken 16-18, DK-2740 Skovlunde, Denmark.

Table1. Basic demographic data of the study subjects

| | | |
|-----------------------------------|----------|-----------|
| Total number | | 18 |
| Average age mean (SD) (year) | | 36.7±13.3 |
| Injury duration mean(SD) (month) | | 14.9±12.3 |
| Injury level | Cervical | 13 (72%) |
| | Thoracic | 5 (28%) |
| ASIA scale | A | 9 (50%) |

| | |
|---|-----------|
| B | 5 (27.8%) |
| C | 3 (16.7%) |
| D | 1 (5.5%) |

ASIA: American Spinal Injury Association

Table2. Video-urodynamic study parameters before and one month after BoNT/A injection

| | Before | After | Mean reduction percentage % | p value |
|--------------------------------------|-------------|------------|-----------------------------------|---------------|
| Pdet (cmH ₂ O) | 75.6±23.8 | 66.8±26.6 | 12.0±27.9 | .054 |
| Plp (cmH ₂ O) | 85.3±35.4 | 78.0±26.9 | 5.5±11.7 | .376 n=15* |
| Dynamic Pure (cmH ₂ O) | 87.0 ±50.0 | 55.1 ±33.3 | 20.4 ±21.0 | .023 † |
| IEMG (μV) | 16.8 ±19.3 | 6.4 ±3.2 | 41.0±44.3 | .008 † |
| Static Pure (cmH ₂ O) | 134.4 ±38.1 | 100.8±26.5 | 21.6 ±23.1 | .012 † |

Abbreviations: Ped, detrusor pressure; Plp, detrusor leak point pressure; Pure, pressure; IEMG, integrated electromyography.

* There are 15 patients who obtained leak point pressure measurement.

Data is shown as mean± SD † $p < .05$

Table3. Post-voiding residual at baseline and on 1st, 2nd, 3rd, and 6th month post-BoNT/A injection

| | Original values (ml) | Mean reduction percentage (%) |
|--------------|----------------------|-------------------------------|
| Baseline | 292± 112 | |
| First month | 178 ± 105*† | 37.1 ± 28.1 |
| Second month | 171± 80*† | 34.0± 30.8 |
| Third month | 198 ± 121* | 30.6 ± 35.8 |
| Sixth month | 281 ± 143* | 23.1± 31.4 |

Data is shown as mean ± SD

* $p < .05$ as compared to baseline

† $p < .012$ (Bonferroni correction of p value) as compared to baseline

LEGEND

Figure1. (A)Ultrasound probe in rectum for perineal injection needle guidance. (B)Trans-rectal ultrasound (sagittal plane) demonstrates hypo-echoic external urethral sphincter (arrow) and hyper-echoic injection needle (arrowhead).

Figure2. Curves of cystourethrometrography from a patient before (A) and after (B) BoNT/A injection. Pves: intra-vesical pressure; Pabd: intra-abdominal pressure; Pdet: detrusor pressure; Pure: urethral pressure; EMG: raw EMG signal; IEMG: integrated EMG.

計畫成果自評

(一) 研究內容與原計畫相符程度

原先預計收集約 20 位病患，最後收集達 18 位病患，但實驗結果仍然有明顯效果。原先預計以 t -test 計算統計顯著性，但因所得數據皆未符合常態分佈，所以使用的統計方法都為無母數統計方法。其餘研究內容均與原計畫相符。

(二) 達成預期目標情況

本研究已明確顯示直腸超音波引導下，直接於會陰部注射肉毒桿菌毒素可以明顯降低病患的殘尿量，及減少病患的尿道壓，且殘尿量減少可持續六個月。但尿動力學檢查顯示最大逼尿肌壓力及漏尿時膀胱內壓沒有明顯變化，可能的原因為尿動力學追蹤的時間太短，或病患人數太少。下次如要進行類似研究，應該在注射後三個月及六個月繼續追蹤尿動力學檢查或增加研究個案。

(三) 研究成果的學術或應用價值

本研究結果顯示在直腸超音波引導下，直接於會陰部注射肉毒桿菌毒素可以有效治療脊髓損傷病患的逼尿肌尿道外括約肌共濟失調，使尿道外括約肌放鬆，並減少殘尿量。殘尿量的減少，可以使病患發生尿道感染的危險性降低，進一步可以保護腎臟，避免慢性腎衰竭。且因為此方法不必由內視鏡來施打肉毒桿菌毒素，可由非泌尿科醫師，尤其是照顧脊髓損傷病患的第一線醫師—復健科醫師來進行，且不用進行麻醉，將可增加病患的便利性及安全性。

(四) 是否適合在學術期刊發表

本研究方法正確，結果有臨床應用價值，現已開始撰稿，將投稿國外雜誌。