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# The effect of a new syringe design on the ability of rheumatoid arthritis patients to inject a biological medication

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ABSTRACT

Self-administration of new biological medications can be difficult for Rheumatoid Arthritis patients with functional impairment and hand and dexterity limitation. Twenty-three Rheumatoid Arthritis (RA) patients participated in this study to compare preferences and injection forces using a conventional syringe and a new ergonomically designed syringe.

Injection force measurements were collected in two ways: a) isometric forces, with the syringes' plungers in fixed positions (depressed halfway and fully depressed), and b) forces exerted during injection of the medication. Subjects' grip and pinch strengths were measured. A perception questionnaire gauged subjects' impressions and preferences.

Subjects were capable of exerting significantly higher isometric forces using the new syringe with the plunger fixed both halfway and fully depressed. During injection of the medication, peak and mean injection forces were significantly higher, and duration was shorter, when using the new syringe. Subjects rated the new syringe higher on all twenty attributes on preference and performance. Therefore, it is expected that the new syringe will benefit self-administration of medication injection for RA patients.



## 1. Introduction

Rheumatoid Arthritis (RA) is a systemic disease that causes inflammation of the membrane lining of the joints, causing pain, stiffness, and swelling of joints (Lipsky, 2008). Early stages of the disease typically affect the function of small joints, such as the fingers and toes. Deformity and pain in the fingers and thumb limit grip and pinch forces (Chacko and Rozental, 2008; Toledano et al., 1992), severely impairing the daily living activities of patients (Helmick et al., 2008).

RA affects nearly 1.3 million people in the United States. Worldwide prevalence is estimated at more than 20 million people. A growing number of biological medications are being developed for the treatment of various medical conditions and diseases. Advantages of biological medications include increased target specificity, greater efficacy and less frequent dosing. The later may enhance patient compliance with the prescribed medications (Shire et al., 2004).

Examples of novel biological medications used for the treatment of RA include the TNF inhibitors (etanercept, infliximab, adalimumab, golimumab and certolizumab pegol), rituximab, tocilizumab, and abatacept. Biologic treatments for RA are administered either by intravenous infusion or by subcutaneous injection. Intravenous infusion is performed at a health care center and can last between 0.5–4 or more hours per session. Some RA medications are self-administered at home via subcutaneous injection.

The shift to self-administration of these new biological medications in the patient's home, however, may demand more careful understanding of patient's ability to self-inject. RA patients have limited hand strength and dexterity, typically experience pain and functional limitations, and often have difficulty performing the injection. Considering that RA is a progressive condition and that functional impairment can increase over time, self-injection can become more challenging.

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Currently there are two options for self-administration of new biological medications: conventional syringes and auto-injectors. Although auto-injectors can overcome some of the problems associated with limited dexterity, they can have their own set of problems, including pain when injecting, misfiring, and uncertainty if the full dose was administered. Consequently, they are not suitable for all patients, with many preferring to use syringes. Conventional syringes, therefore, need to be redesigned in order to address RA patients' dexterity limitations and functional impairments, and to facilitate self-administration of new biological medications. The goal of this study is to investigate application of a new ergonomically designed syringe for RA patients and determine if syringe design improves patients' ability to self-administer new biological medications.

## 2. Method

### 2.1. Subjects

Twenty-three RA patients, 10 females and 13 males, ages 26 to 74, participated in the study (see Table 1). One subject who participated in study however presented concern about using syringe with actual medication during actual injection. Subjects were recruited in New York City by an independent market research company, and were asked to participate based on a telephone screening questionnaire. During a telephone interview, subjects were asked to rate their severity of RA as mild, moderate, and severe. The inclusion criteria specified subjects exhibiting mild, moderate, and severe levels of rheumatoid arthritis, and who have been taking injectable medication for 3 to 24 months. Subjects had no physical disability, aside from the effects of RA, which would prevent them from using injection products. Subjects who fulfilled the inclusion criteria based on the telephone screening interview were invited to participate, and were scheduled for an individual interview and evaluation session one month after the phone screening. The subjects were informed that the interview session was being conducted strictly for research proposes, they would receive an honorarium for their participation, and they would not be asked to purchase any products or to inject any medication into their bodies.

**Table 1**
Subject demographic information.

| | |
|---|---|
| Years since diagnosis | 1 to 11 years |
| Experience with injectable medication | 3 to 12 months |
| Gender ($n = 23$) | |
| Males | 59.1% (13 subjects) |
| Females | 40.9% (10 subjects) |
| Age | |
| 18–30 | 4% |
| 31–40 | 13% |
| 41–50 | 26% |
| 51–60 | 43% |
| 61–70 | 9% |
| 70+ | 4% |
| RA Medication used at time of survey | |
| Etanercept | 52% |
| Adalimumab | 22% |
| Infliximab | 4% |
| Other (None anti-TNF medications) | 22% |
| Self reported RA severity | |
| Mild | 30% (7 subjects) |
| Moderate | 35% (8 subjects) |
| Severe | 35% (8 subjects) |
| Classification of RA patients' severity by rheumatologist | |
| Mild | 35% (8 subjects) |
| Mild to moderate | 35% (8 subjects) |
| Moderate | 22% (5 subjects) |
| Moderate to severe | 8% (2 subjects) |
| Severe | 0% (0 subjects) |

### 2.2. Syringe specifications

Two pre-filled syringe designs were used in the study to assess the effect of design on the ability of RA subjects to perform injections. Injections were performed using simulated skin pads. One syringe, referred to as the RAPID 2 syringe (R in Fig. 1), is a standard pre-filled "off-the-shelf" syringe, comprised of a flat thumb pad, a plunger rod, a finger flange, a glass barrel, and a needle cap. R syringe was used in a clinical study (Smolen et al., 2009), "RAPID 2 study", for self-administrated injection of medication. The second syringe, referred to as the N syringe, is a new ergonomically designed syringe with an indented rubber thumb pad, a sturdy plunger rod, an elongated finger flange, an oval plastic barrel or sleeve, and a specially designed needle cap. The N syringe was created by Smart Design, OXO International, and UCB Celltech.

The R and N syringes use the same glass barrel and needle, prefilled liquid, and internal rubber stopper attached to the plunger rod (Fig. 1). UCB Celltech provided one ml long glass syringes prefilled with certolizumab pegol, a PEGylated Fab' anti-TNF. Syringes were transported together to the usability testing site and were kept at ambient room temperature. The syringes included a 25 G, ½ in long, thin-wall staked needle for subcutaneous administration.

### 2.3. Protocol for the study sessions

Subjects were interviewed one at a time. Each interview session began with an explanation of the objectives of the study and the procedures for the session. Subjects were reminded that their session would be videotaped. They were then asked to sign

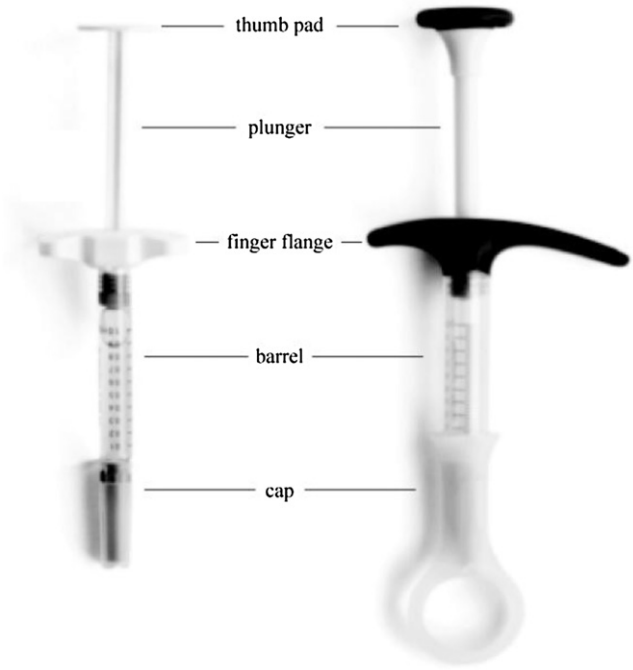


**Fig. 1.** The R (left) and N (right) syringe designs used in the study.

a consent form, approved by UCB and GfK V2 (an independent market research company).

The first part of the session consisted of gathering information about the severity of the patient's RA, and his or her medication history. Data collection methods included a questionnaire, the Cochin Scale of disease severity, a hand and finger symptom survey, and photography of the subject's hands to confirm severity of RA after interview and testing session.

An independent consultant rheumatologist was used to analyze the respondent's disease severity. Photographs of the respondent's hands, along with completed validated questionnaire (The Cochin Scale) by the respondent were analyzed by the rheumatologist, along with their measured grip strength data (obtained using a dynamometer) in order to confirm the severity of their disease following the interview and testing session.

Subjects were asked to describe any functional limitations and pain associated with their hands and fingers, generally and specifically, as related to their RA medical condition. The Cochin Scale, designed to score functional ability and disability of RA patients, is based on ratings of 18 daily activities such as working in the kitchen (8 questions), dressing (2 questions), hygiene (2 questions), working at the office (2 questions), and other general activities (4 questions).

Subjects rated the ease or difficulty of each activity using a Likert-like scale that ranged from 0 (performed without difficulty) to 5 (impossible to do). The ratings were totaled to provide an overall score for each patient (Bell et al., 1990). Sensitivity of the Cochin scale to the stage of the disease (Fries et al., 1982), and its testing reliability and validity, have been demonstrated (Bell et al., 1990).

### 2.4. Subjects' perception ratings of the syringes

Next, the subjects were asked to rate their impressions of the two syringes at three different times: 1) when seeing photographs of the syringes for the first time, 2) after holding and examining each syringe, and 3) after using each syringe in a simulated injection. The syringe evaluations therefore began by collecting initial perceptions. Subjects were shown photographs of each syringe, presented in random order, and asked to give their impressions based on the photographs and descriptions of the features of each syringe. Following this, the syringes were displayed (at this point, with the needles removed for safety). Subjects were asked to pick up each syringe to feel and hold it. The subjects were again asked to give their impressions.

Printed instructions for injection were then presented. Following the two injections, subjects were asked to discuss their overall impression of each syringe. They then performed a final evaluation by rating their opinions of the two syringes. Subjects rated each syringe according to 20 different design attributes. The attributes were presented as semantic differentials, in which opposite qualities describe two ends of a scale. Nineteen of the attributes included questions such as willingness to inject ("Very unwilling"/"Very willing"), control (Difficult to control/Easy to control), and comfort (Uncomfortable/Comfortable). Using a 7-point scale, subjects recorded their opinions, 1 was the worst and 7 the best rating.

### 2.5. Force measurements

To characterize each subject's physical abilities, three types of force measurements were collected:

a) Grip and pinch strength abilities,
b) Maximum isometric forces applied to each syringe, and
c) Forces applied to each syringe during injection of the medication.

A MicroFet 4 dynamometer was used to measure maximum hand grip, two-point pinch, and lateral/key pinch forces, and for strength measurements. The subject's elbow was positioned at the side of trunk and flexed 90 degrees. Three trials were conducted, each lasting 5-seconds, with at least 2-minute rest in between each trial. The strength measurements were performed in random order.

In order to investigate the effect of syringe design on maximum force exertion during injection, in addition to standard strength measurements previously, maximum isometric force was measured during two specific points during actual injection posture. For each syringe, the plunger was fixed at two positions: at halfway and at it's lowest (fully depressed) position. The order of the positions was randomized. Subjects were asked to use the syringe with their thumb at the top of the plunger pressing as hard as possible for 5-seconds. Three trials were collected. Testing posture was close to one recommended for actual self-injection. It was expected that these isometric data provide more realistic effect of syringes on biomechanical characteristics of force exertion during actual injection, and demonstrate relevance of these forces to forces measured by standard maximum grip, two-point pinch, and lateral/key pinch forces.

Subjects were asked to use each syringe by injecting the medication into a simulated skin pad that was placed on their thigh. The order of the syringes was randomized. The instructions consisted of pictures and text given to the subject to explain the process of injection, see Fig. 2. The process included cap removal, inspection for air bubbles, the recommended 45°-degree injection

**Fig. 2.** Pictures used to demonstrate injection instruction to subject with narrative suggesting to hold the syringe in a way that is comfortable to insert the needle into the injection site for the whole length of the needle at about 45° to surface of the artificial skin.

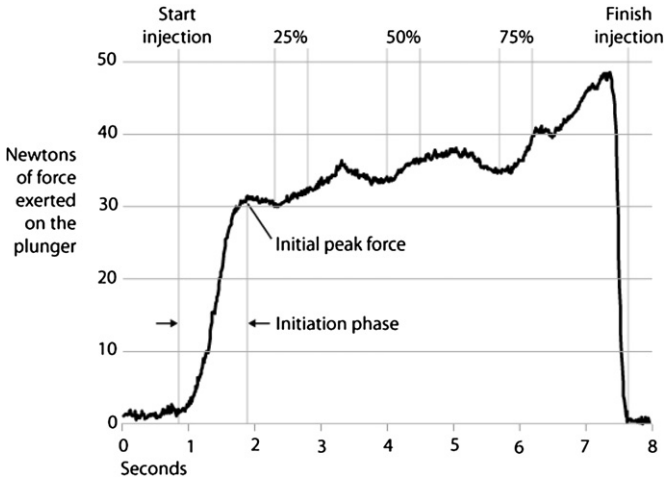


**Fig. 3.** Segments of trace used for analysis of forces applied during a typical injection.

angle into the skin pad, and insertion of the needle to initiate the injection. Force measurements were recorded throughout the entire injection. No instruction was provided with respect to time required to complete the injection phase. Force applied during injection of medication was measured continuously using FlexiForce transducers (Tekscan, Inc., Boston MA). The FlexiForce transducers were placed within the syringe plungers' thumb piece. The transducers were connected to Data Acquisition cards (DAQcard 6036E, National Instruments) and a laptop computer (Dell Latitude D600). The data was collected by LabView 8.1 software (National Instruments, Austin, TX). The software collected data from the FlexiForce sensors at a rate of 100 H.

To ensure accuracy and reliability of measurements, the FlexiForce transducers were attached to the plunger rod in a way that provided consistent surface contact with the sensor. The transducers were then calibrated using SQ General Purpose Ohaus Champ™ Industrial Bench Scale (Ohaus, Pine Brook, New Jersey) and digital scale. Known weights were placed on the plunger tips while the plungers were positioned on the digital scale. The regression method was used to establish a conversion equation for each sensor used in the study. The measurements were repeated to ensure validity of the conversion factors.

### 2.6. Processing of the force data

A measure of interest is the rate at which subjects are able to reach "full force" at the start of injection. For each subject the maximum slope and the average slope, from the point of initial application of force until "full force" exertion, were extracted from the data (see Fig. 3). "Full force" was defined as the instant a peak force value was first observed, after which the force either dropped or remained constant. Forces exerted during the injection were collected continuously. Forces at three points in time were included in the analysis: 25%, 50%, and 75% through the injection period (Fig. 3). Those points were arbitrarily selected to analyze the pattern of force exertion during the actual dynamic injection. In calculating other force measurements, a sample of 50 sequential measurements was averaged, representing a half-second interval, to obtain a stable value (rather than using a single 1/100th of a second measure).

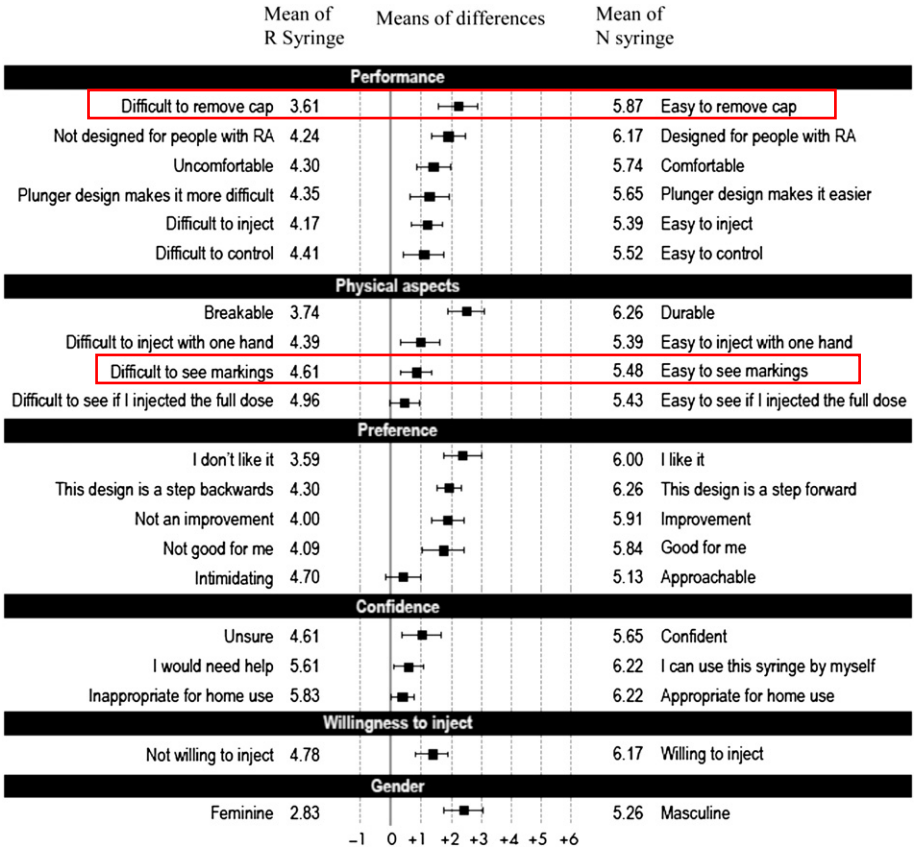


**Fig. 4.** Mean scores rated on a 7-point likert-like scale for two syringes based on twenty attributes.

**Table 2**
Mean and standard deviation (SD) of force during actual and isomeric injection by severity.

| Syringe | R | | | N | | |
|---|---|---|---|---|---|---|
| Task | Actual injection | Maximum isometric injection forces with the plunger halfway depressed | Maximum isometric injection forces with the plunger fully depressed | Actual injection | Maximum isometric injection forces with the plunger halfway depressed | Maximum isometric injection forces with the plunger fully depressed |
| Severity | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) |
| Mild | 2.92 (0.85) | 5.27 (1.84) | 4.63 (1.46) | 3.41 (1.49) | 8.01 (3.23) | 7.04 (3.34) |
| Moderate | 2.29 (0.79) | 3.49 (1.33) | 2.98 (1.98) | 2.84 (1.14) | 4.53 (2.23) | 3.58 (2.98) |
| Severe | 1.75 (1.01) | 3.54 (2.03) | 2.93 (1.94) | 2.30 (1.45) | 5.39 (3.58) | 3.85 (2.06) |

### 2.7. Statistics

The paired *t*-test was used to evaluate the differences in characteristics of forces and the Wilcoxon Signed Ranks Test was used for preferences of the R and N syringes. The correlations between grip and pinch strengths, and isometric force capabilities measured by the plunger fixed at a halfway position were calculated to provide information about the relationship between isometric force capability as measurements with instrument syringe and standard clinical testing of the isometric capabilities.

Two-way analysis of variance (ANOVA) was used to test the effects of syringe design (N and R syringes) and plunger position (halfway and fully depressed position) and their interaction with maximum isometric force. Another two-way ANOVA examined the effects of syringe design (N and R syringe), the three points during the injection (25%, 50%, 75% of injection time), and their interaction with dynamic injection force. A Tukey post hoc test was performed when the multivariate test was significant ($p < 0.05$). The outcomes were analyzed by using the Statistical Package for the Social Sciences (SPSS™, version 15.0, Chicago, IL).

## 3. Results

### 3.1. Severity of arthritis

Based on assessment of photographs of the patients' hands, and results from the Cochin Scale, subjects in this study were classified by the rheumatologist as follows: 8 (36.4%) mild, 8 (36.4%) mild-to-moderate, 5 (22.7%) moderate, and 2 (4.5%) moderate-to-severe. None of the subjects were in the severe category, (Table 1).

Severity of arthritis, as classified by the rheumatologist, had significant effect on isometric force applied to the halfway ($p = 0.040$ for R and $p = 0.011$ for N) and fully depressed plunger ($p = 0.021$ for R and $p = 0.007$ for N) positions, see Table 2. However, severity of arthritis had no statistically significant effect on mean and maximum forces exertion during the injections.

### 3.2. Perception ratings of syringes

Of twenty attributes presented, nineteen had positive or negative connotations. Of the twenty attributes, 15 were statistically significant at the 95% confidence level, and 16 were statistically significant at the 90% confidence level. With respect to attributes related to performance, subjects reported that the N syringe was more comfortable (R device 4.2 (1.7) vs. N device 6.0 (1.0)) and easier to inject (R device 4.0 (1.8) vs. N device 5.5 (1.3)). With respect to attributes related to force production, subjects reported that the N syringe provided more control (R device 4.4 (2.0) vs. N device 5.5 (1.7)), was designed for arthritis patients (R device 4.2 (2.1) vs. N device 6.2 (1.4)), and the plunger had a better design that made injection easier (R device 4.3 (2.0) vs. N device 5.7 (1.7)). With respect to preference, subjects liked the N syringe better (R device 4.7 (1.9) vs. N device 6.3 (1.1)) and disliked it less (R device 3.4 (2.1) vs. N device 6.2 (1.0)).

### 3.3. Grip and pinch strength measurement

Table 3 presents means and standard deviations of hand grip, lateral/key pinch, and two-point pinch forces. Patients were able to exert greater force using the two-point pinch, 191.92 N (73.94), compared to the lateral/key pinch, 99.64 N (39.32). Table 3 shows their correlation coefficients with the maximum forces exerted with the plungers fixed at a halfway position, for both the N and R syringes. The correlation coefficients show that patients' maximum hand grip, lateral/key pinch, and two-point pinch forces all correlate.

### 3.4. Isometric force measurements

Of the 22 subjects that completed the isometric force test with the plunger halfway depressed, 17 exerted more force when using the N syringe, one subject exerted approximately equal forces for both syringes, and four subjects exerted more force using the R syringe (see Fig. 5). Sixteen subjects performed the isometric force test with the plunger in the fully depressed position. Of these, 11 subjects exerted more force when using the N syringe, two subjects applied approximately equal forces, and three subjects exerted more force using the R syringe (Fig. 5). Due to technical error, the isometric force test with the plunger in the fully depressed position was not performed on the first six subjects.

Fig. 6 shows means and standard deviations for the maximum isometric force with the plunger fixed at the halfway down and fully depressed positions for each syringe. In each position, subjects demonstrated significantly higher mean and maximum isometric forces ($p < 0.001$) using the N syringe. The maximum isometric force was higher with the plunger depressed halfway than when it was fully depressed. With the plunger halfway depressed, the R syringe

**Table 3**
Means and standard deviations of hand grip, lateral/key pinch, and two-point pinch forces, and their correlation coefficient with isometric force capabilities measured by the plunger fixed at a halfway position.

| | Mean (SD) | R syringe | N syringe |
|---|---|---|---|
| | | Correlation | Correlation |
| Hand grip | 578.59 N (274.78) | 0.699* | .717* |
| Lateral/key pinch | 99.64 N (39.32) | 0.763* | .818* |
| Two-point pinch | 191.92 N (73.94) | 0.744* | .770* |

Note: * indicates correlation coefficient significance at $p < 0.002$.

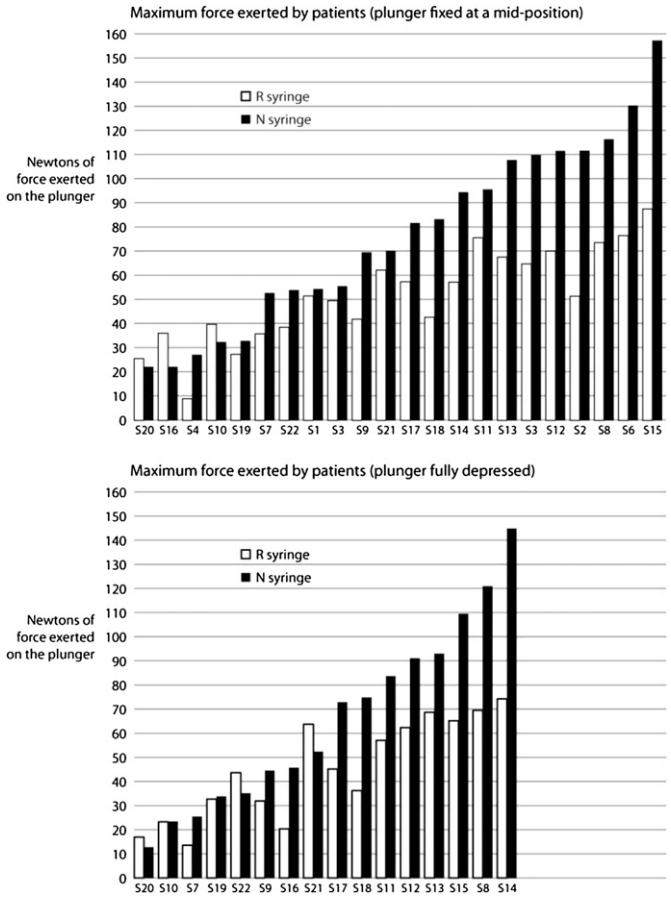


**Fig. 5.** Isometric forces applied to the syringes by each subject, with the plunger fixed at halfway position, and fully depressed. The data in graph sorted by the force output level for easier visual comparison.

averaged 51.99 N (19.33), while the N syringe averaged 77.11 N (38.26). With the plunger fully depressed, the R syringe averaged 45.30 N (20.28), while the N syringe averaged 66.51 N (38.52). Both main effects of syringe design ($F = 14.974$, $p = 0.002$) and plunger position ($F = 4.807$, $p = 0.045$) were statistically significant. The effect of syringe design was greater than the effect of plunger position. The interaction effect was not significant ($F = 0.075$ $p = 0.405$).

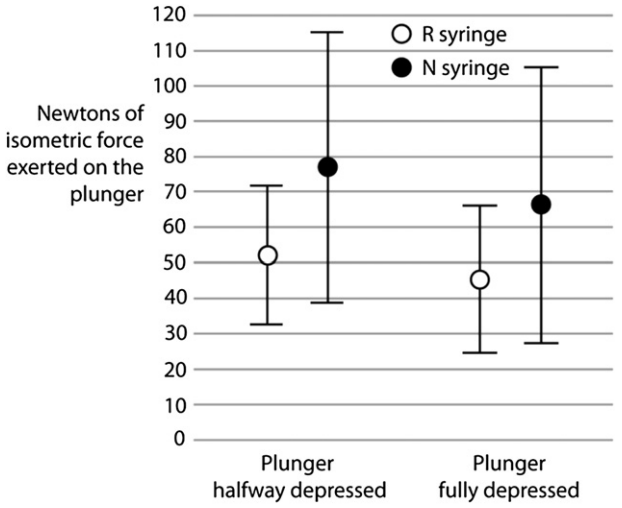


**Fig. 6.** Maximum isometric injection forces with the plunger halfway depressed and fully depressed, for the R and N syringes.

### 3.5. Injection force measurements

When subjects injected medication into the simulated skin pad, both the maxima and means of the peak forces, as well as the mean slopes during the initial phase of injection, were significantly higher for the N syringe compared to R syringe (Table 4). The duration of the entire injection was also significantly shorter with the N syringe. The duration of initial slope was not proven to be significantly different.

Fig. 7 shows the means and standard deviations of forces collected at three points during the injection period: 25%, 50%, and 75%. The effects of these points during injection period ($F = 4.726$, $p = 0.027$) and syringe design ($F = 8.018$, $p = 0.010$) were statistically significant. The interaction effect was not significant ($F = 0.455$, $p = 0.574$). The force at 25% was smaller ($F = 9.382$, $p = 0.006$) than that at 50%. There was no difference ($F = 0.873$, $p = 0.361$) between injection forces at 50% and 75%.

## 4. Discussion

This study reports on rheumatoid arthritis patients' perceptions and performance capabilities of a newly designed syringe. While the patients who participated in the study had prior experience with subcutaneous injection of medications, they had never been exposed to the medication or the new ergonomically designed syringe used in this study. The new, ergonomically designed N syringe had high acceptance among more patients. Patients were able to exert greater force using the N syringe compared to the R syringe, which was a traditional off-the-shelf syringe. The new ergonomic syringe may therefore improve RA patients' control and comfort and hence facilitate self-injection.

Several factors may influence the force that patients exert during injection. Grip and pinch forces of healthy subjects are reported to be affected by: gender (Dempsey and Ayoub, 1996), pinch type (Dempsey and Ayoub, 1996), pinch width (Dempsey and Ayoub, 1996), muscle length, muscle and tendon compliance (Loren et al., 1996), joint conditions (Berme et al., 1977), neurological problems (Boissy et al., 1999), and relevant body/joint configuration (Balogun et al., 1991; Li, 2002). While some of these factors may help predict the forces produced during injection, the use of a syringe might present a more complex task compared to grip and pinch force. Results of this study suggests that force exerted during injection may partially be explained by other factors such as hand grip, lateral/key pinch, and two-point pinch forces (see Table 3).

The R syringe is a traditional syringe with a small flat flange, providing space for one finger at each side of the flange, each exerting force in opposition to the thumb force on the plunger. In contrast, the N syringe represents a more ergonomically and patient-friendly syringe that provides a larger diameter thumb plunger, incorporating a rubber-like cover, and a longer, curved finger flange with smooth edges. Its finger flange is asymmetric; with one side long enough to accommodate two fingers underneath. This enables patients to use three fingers to oppose the thumb, and thereby apply more force during injection.

Previously there has been no information demonstrating the importance of including additional fingers to increase a patient's ability to inject medication. The results of the isometric force tests in this study demonstrated that patients produced approximately 40% more force using the N syringe with the plunger at halfway position, and 39% more force with the plunger fully depressed. Furthermore, subjects reported that the N syringe provided more control, making the injection of the medication easier than with the

**Table 4**
Forces and duration during injection of medication using the R and N syringes.

| | Unit | R mean | N mean | Difference N − R | *p*-Value (2-tailed) |
|---|---|---|---|---|---|
| | | R Std. deviation. | N Std. deviation. | | |
| Total work (area under the curve) | Newtons × seconds | 346.12 (102.86) | 372.46 (75.26) | 26.34 (123.12) | 0.33 |
| Duration of the initiation phase | Seconds | 4.77 (4.08) | 3.28 (1.50) | −1.49 | 0.14 |
| Duration of the entire injection | Seconds | 19.85 (13.76) | 18.48 (9.84) | −1.36 | .031 |
| Average increase in force during the initiation phase | Newtons/second | 8.5 (6.11) | 13.44 (9.88) | 4.93 (9.31) | 0.01 |
| Maximum increase in force during the initiation phase | Newtons/second | 18.70 (9.69) | 30.38 (21.61) | 11.68 (17.89) | 0.01 |
| Average force applied during the injection | Newtons | 22.49 (9.65) | 27.70 (13.61) | 5.20 (8.79) | 0.01 |
| Maximum force applied during the injection | Newtons | 33.12 (11.94) | 45.34 (20.58) | 12.22 (13.60) | 0.001 |

R syringe. The findings of this study therefore show that the larger, curved flange, allowing inclusion of an additional finger during injection, provides a more patient-friendly syringe and enhances their force production and ability to self-inject medication.

Subjects were capable of exerting forces during injection when using the N syringe which were on average 36% of their maximum isometric effort when the plunger was in a fixed position, halfway depressed. For the R syringe, forces averaged 43% of their maximum isometric effort. Utilization of a smaller percentage of maximum effort is generally associated with increased ability to control the force and increased comfort during performance of a task. This may provide reasonable explanation for the subjects rating the N syringe more favorably than the R syringe.

During injection, subjects were able to exert an initial peak force that was 54% higher (28.05 N/18.24) with the N syringe compared to the R syringe (12.45 N/8.34). It took less time for subjects to reach their initial peak force when starting the injection. The N syringe also resulted in shorter overall injection times. As expected, with the medication being injected, the patterns of force observed at 25%, 50%, and 75% through the injection were similar for the N and R syringes, showing no statistically significant difference. The results suggest however that the N syringe will assist patients to overcome the initial phase of injection faster than the R syringe. Additionally, in view of their maximum isometric force capabilities, patients will be able to maintain the required injection force using relatively less effort.

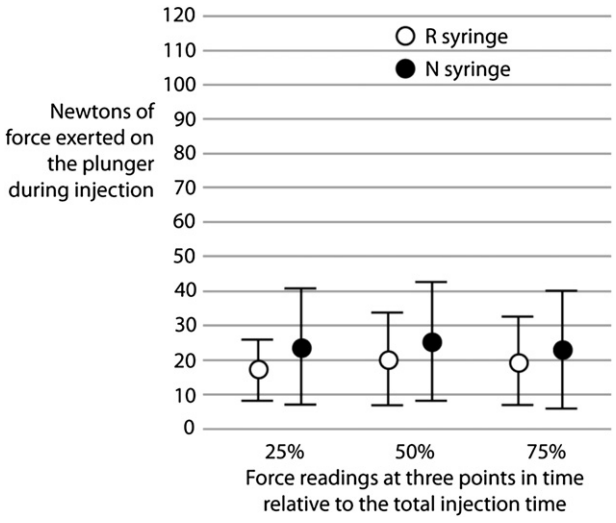


**Fig. 7.** Dynamic injection force at 25%, 50% and 75% during injection period with R and N syringes.

In this study RA patients' maximum isometric capabilities were significantly affected by the severity of their arthritis. However, the maximum and average applied force during injection was not statistically different during actual injection. Deformity and pain in the fingers and thumb has been reported to affect RA patient's grip and pinch forces (Chacko and Rozental, 2008; Toledano et al., 1992). Table 3 demonstrates the results of clinical force measurements of hand grip, lateral/key pinch, and two-point pinch, and their correlation coefficients with isometric force.

The success of a new design should be judged based on both an increase of overall performance and overall acceptance of the new design by the end user. Subjects rated all attributes related to performance and physical aspects of the new syringes more positive for the N syringe than the R syringe (see Fig. 4). The results demonstrate that subjects were more willing to inject with the new syringe, more confident during injection, and found it easier to inject with the N syringe compared to the R syringe.

### 4.1. Study limitation

This study used a small group of RA patients based on patient's perception of RA severity. A rheumatologist was asked to provide clinical ratings of RA severity for each subject based on survey information and hand photography. It is important to note that the self-reported severities and rheumatologist's classification of patients' severities is different, see Table 1. The subject's self-reported ratings of RA may include all body parts (i.e. arms, legs, ankles, feet) whereas the rheumatologist's assessment was based on photography of the subject's hands and other survey information, without direct patient communication.

The current study only used one position for subcutaneous injection, simulating injection in the upper thigh with patients in a seated position. Patients, however, are instructed to inject either in the lower abdomens or upper thigh. Using a different injection site will affect overall upper extremity posture and performance, and specifically wrist and finger capability, and thereby affect the ability to inject. However, it is expected that patients using different positions will experience performance differences for the N and R syringes similar to those seen here, and other positions will only effect the magnitude of force and not affect the overall findings of this study.

Subjects in this study had prior experience with injectable medications and therefore had previous experiences and different styles of injection, i.e., methods in which they positioned their head, trunk, and shoulder posture. This study recommended a specific needle angle and location of injection. No attempt was made to control the subjects' trunk and shoulder posture during injection. However, the authors believe that such variables in posture or style of injection is the result of the subjects' experience

with injectable medication, and is not due to an experimental learning effect (i.e. not an effect of the order of testing or the subjects' familiarity with the R and N syringes).

The R and N syringes incorporated identical mechanical parts (i.e., they used the same glass barrel and needle, prefilled liquid, and internal rubber stopper). Subjects in this study were introduced briefly to both syringes and they were asked to use these syringes and rate them. Long term experience with these syringes may alter their rating and preference.

## 5. Conclusion

Subcutaneous injection of medications may present a special challenge for specific groups of patients that have limited hand/finger strength, and/or limited dexterity. Pharmaceutical companies should carefully evaluate the functional capabilities of patients who are self-injecting such medications. Severity of diseases effects maximum patient capabilities for applying force. Consideration of more patient-friendly and ergonomically designed syringes may enhance subjects' ability to overcome specific aspects of their functional limitations and consequently may help improve compliance and result in a better overall injection experience as a means of drug delivery methods.

### Conflict of interest

The study was funded by UCB, Inc. UCB contributed to the study design, and the collection in collaboration with GFK US healthcare, LP, analysis and interpretation of the data.

### Authors Disclosure

A. Sheikhzadeh: Yes; UCB: Research Support, J. Yoon, Yes UCB: Research Support, D. Formosa: Yes; UCB: Consultant, B. Domanska: Yes; UCB: Employee, D. Morgan: Yes; UCB: Employee, M. Schiff: Yes; UCB: Research Support; UCB: Consultant.

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