LONGITUDINAL NON-INVASIVE FOLLOW-UP OF CHANGES IN URINARY BLADDER FUNCTION SECONDARY TO BENIGN PROSTATIC ENLARGEMENT. RESULTS OF THE FIRST OBSERVATION INTERVAL.

Hypothesis / aims of study
With increasing age, the prostate of most men enlarges (benign prostatic enlargement, BPE). In an early stage the urinary bladder contractility presumably increases to compensate for the increase in resistance to urinary flow. In a later stage the urinary bladder may become damaged to such a degree that effective bladder emptying is not possible, which is called “decompensation”. The onset of irreversible bladder damage is poorly defined, but very important when making a therapeutic decision in BPE. As BPE develops over a long period of time, it is necessary to obtain reference data from a group of healthy men during a period of 40 years (age 40-80 years). For practical reasons we study a group of male volunteers stratified in 8 age cohorts during a shorter period. Each cohort will undergo 3 non-invasive urodynamic investigations in 5 years. Subsequently each cohort will have the age of the previous cohort at inclusion, and results will be matched. To measure bladder pressure, the non-invasive condom catheter method is used. Presently, 2 investigations have been completed and the first follow-up results are presented in this report.

Study design, materials and methods
Between 2001 and 2006 754 male volunteers underwent 2 non-invasive investigations [1]. Inclusion criteria were: age 38 to 77 years, the ability to continuously void in a standing position with a minimum flow rate of 5.4 ml/s, no history of any heart condition, no treatment or surgery of the lower urinary tract (LUT) and no other disease that could affect urinary bladder function. LUTS were present as median (Inter Quartile Range, IQR). Differences between strata were tested using the non-parametric Kruskal-Wallis (KW) test or Mann-Whitney (MW) test. Changes between the first and the second investigation were tested using the non-parametric Wilcoxon signed Rank (WR) test. Linear Regression was used to test relations between parameters.

Results
Cross-sectional analysis of the first investigation showed that with increasing age, prostate volume significantly increased from 25 cm³ to 45 cm³ (KW p<0.05). In addition, symptom score significantly increased from 4 to 6 (KW p<0.05), whereas maximum flow rate decreased from 20 ml/s to 12 ml/s (KW p<0.05). Linear regression confirmed a significant age-dependence of these 3 parameters. Maximum condom pressure did not depend on age (KW p=0.37).

In an observation interval of 31 months prostate volume (PV, cm³) was determined by transabdominal ultrasonography (Aloka SSD-900, 3.5 MHz probe) [3]. The volunteers were also asked to complete the IPSS questionnaire.

For data analysis, the volunteers were first stratified in five year agegroups to study the age dependency of the urodynamic parameters. Subsequently, a stratification in prostate volume groups and maximum flow rate groups was done. Data were presented as median (Inter Quartile Range, IQR). Differences between strata were tested using the non-parametric Kruskal-Wallis (KW) test or Mann-Whitney (MW) test. Changes between the first and the second investigation were tested using the non-parametric Wilcoxon signed Rank (WR) test. Linear Regression was used to test relations between parameters.

The table below shows 5 strata of prostate volumes. Volunteers with a prostate volume larger than 42 cm³ (n=152) at inclusion had a significantly lower maximum flow rate (13.8 (9.0) ml/s vs 16.2 (10.6) ml/s, n=602), MW p<0.05) and a significantly higher symptom score (MW p=0.03) than the volunteers in the other prostate volume cohorts. In an observation interval of 31 months the changes in the listed parameters were similar in all prostate volume cohorts. However, in the cohort with prostate volumes larger than 42 cm³ symptom score increased 0.5, which is significantly more than in the other cohorts (MW p=0.02).

The table below shows 5 strata of maximum flow rates. In cross-sectional analysis the cohort with the lowest maximum flow rate at inclusion was associated with a significantly higher con-dom pressure (105 (46) ml/s vs 97 (37) ml/s, n=453), MW p=0.02) and symptom score (6 (6) ml/s vs 5 (6), MW p=0.05) compared to the 3 consecutive cohorts. The change in maximum condom pressure in an observation interval of 31 months strongly depended on the initial flow rate. In the cohort with maximum flow rate between 4.5 and 10.5 ml/s, maximum condom pressure decreased slightly. At higher maximum flow rates maximum condom pressure in-creased up to almost 10 cmH2O in the cohort with a maximum flow rate higher than 23.5 ml/s.

[Table of data]

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PV (cm$^3$) | 32 | 31 | 31 | 29 | 28 | 0.27

Changes after an observation interval of 31 months:

| IPSS2 – IPSS1 | 1 | 0 | 0 | 0 | 0 | 0.13 |
| P$_{\text{cond.max}}$2 – P$_{\text{cond.max}}$1 (cmH$_2$O) | -2 | 7 | 10 | 9 | 10 | <0.05 |
| PV 2 – PV 1 (cm$^3$) | 0 | 1 | 0 | -1 | 0 | 0.35 |

Interpretation of results
The data from this study show that with increasing age the risk of developing LUTS increases, indicated by an increase in prostate volume and symptom score, and a decrease in maximum flow rate. In an observation interval of 31 months, maximum condom pressure increased and maximum flow rate decreased. Both changes were similar in all agegroups. However, the change in maximum condom pressure strongly depended on the maximum flow rate at inclusion. Based on our findings, we speculate that men with a low maximum flow rate and a high condom pressure at inclusion are in the decompensation phase. This is supported by the slight decrease in maximum condom pressure in an observation interval of 31 months in these men. Men with higher maximum flow rates at inclusion who showed an increase in condom pressure in the observation interval of 31 months are probably compensating for an increased urethral resistance. This hypothesis is based on 2 observations with an observation interval of 31 months. More observations in a longer interval are underway.

Concluding message
This study shows the first results of prospectively studying compensation and decompensation of the urinary bladder. In an observation interval of 31 months, changes in isovolumetric bladder pressure and maximum free flowrate were found that are consistent with the hypothesis that in early stages of BPE compensation occurred, later followed by decompensation. The non-invasive condom catheter used in the 2 investigations in a 31 months time interval is very suitable for this purpose.

References