# ProfNet PlagiatService

## -Prüfbericht-

für
Prof. Dr. Joachim Noldus

Münster, den 24.10.2015



# ProfNet PlagiatService - Zusammenfassung

| | |
|---|---|
| Autor | Prof. Dr. Joachim Noldus |
| Titel | Experimental and clinical stud ... |
| Typ | Habilitation |
| Abgabetermin | 31.12.1997 |
| Hochschule | |
| Fachbereich | |
| Studiengang | |
| Fachrichtung | Medizin |
| 1. Gutachter | Prof. Dr. H Huland |
| 2. Gutachter | |
| Prüfdatum | 24.10.2015 |

| | |
|---|---|
| Dateigröße | 108.975 |
| Seiten | 55 |
| Absätze | 238 |
| Sätze | 730 |
| Wörter | 14.115 |
| Zeichen | 78.813 |
| Abbildungen | 0 |
| Tabellen | 0 |
| Fußnoten | 15 |
| Literatur | 0 |
| Wörter (netto) | 14.079 |

| | |
|---|---|
| Abbildungsverzeichnis | ☐ |
| Abkürzungsverzeichnis | ☐ |
| Anhang | ☐ |
| Eidesstattliche Erklärung | ☐ |
| Inhaltsverzeichnis | ☐ |
| Literaturverzeichnis | ☐ |
| Quellenverzeichnis | ☐ |
| Stichwortverzeichnis | ☐ |
| Sperrvermerk | ☐ |
| Symbolverzeichnis | ☐ |
| Tabellenverzeichnis | ☐ |
| Vorwort | ☐ |

| Analysetyp | Indizien |
|---|---|
| Bauernopfer-Absatz | 16 |
| Bauernopfer-Halbsatz | 3 |
| Bauernopfer-Satz | 6 |
| Bauernopfer-Wort | 12 |
| Eigenplagiat | 93 |
| Teilplagiat | 7 |
| Zitierungsfehler | 1 |

Anteil Fremdtexte (netto): 8 % (1.176 von 14.079 Wörtern)

| | |
|---|---|
| Phrase-allgemein | 22 |
| Phrase-fachspezifisch | 17 |
| Zitat-Fremdtext-ohne Quelle | 3 |
| Zitat-im Text-ohne Quelle | 4 |

Anteil Fremdtexte (brutto): 12 % (1.659 von 14.115 Wörtern)

**39%** Gesamtplagiatswahrscheinlichkeit

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Institut für Internet-Marketing

# ProfNet PlagiatService - Ergebnis Textanalyse (alle Analysen)



| Kriterium | Dimension | Prüfdokument | Erstprüfer | Fachbereich | Hochschule | Fachrichtung | Hausarbeiten | Seminararbeiten | Bachelor Thesen | Diplomarbeiten | Master Thesen | Dissertationen | Habilitationen | alle |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dokumente | Anzahl | 1 | 0 | 14 | 1 | 1435 | 391 | 362 | 373 | 2486 | 288 | 23850 | 192 | 340696 |
| Abbildungen | Anzahl (Durchschnitt) | 0 | 0 | 6 | 0 | 4 | 2 | 2 | 7 | 7 | 3 | 5 | 7 | 2 |
| Absätze | Anzahl (Durchschnitt) | 238 | 0 | 895 | 1652 | 300 | 114 | 119 | 253 | 372 | 309 | 555 | 782 | 309 |
| Fußnoten | Anzahl (Durchschnitt) | 15 | 0 | 250 | 111 | 21 | 37 | 46 | 45 | 62 | 48 | 107 | 129 | 32 |
| Literatur | Anzahl (Durchschnitt) | 0 | 0 | 2 | 0 | 13 | 1 | 7 | 10 | 4 | 1 | 6 | 2 | 4 |
| Sätze | Anzahl (Durchschnitt) | 730 | 0 | 2419 | 5670 | 1214 | 493 | 507 | 1020 | 1518 | 1345 | 2409 | 3493 | 1051 |
| Seiten | Anzahl (Durchschnitt) | 55 | 0 | 261 | 438 | 99 | 33 | 32 | 74 | 107 | 95 | 163 | 201 | 64 |
| Tabellen | Anzahl (Durchschnitt) | 0 | 0 | 13 | 28 | 3 | 1 | 1 | 2 | 3 | 3 | 4 | 3 | 1 |
| Wörter | Anzahl (Durchschnitt) | 14115 | 0 | 36980 | 115334 | 19530 | 8139 | 8013 | 16150 | 23773 | 22323 | 38792 | 56546 | 17546 |
| Zeichen | Anzahl (Durchschnitt) | 78813 | 0 | 315711 | 808606 | 133899 | 53847 | 53231 | 106385 | 158421 | 141639 | 258203 | 388159 | 113893 |
| Zitate | Anzahl (Durchschnitt) | 38 | 0 | 409 | 711 | 79 | 80 | 64 | 106 | 163 | 146 | 219 | 347 | 105 |

Die statistischen Ergebnisse der Textanalyse des Prüfdokumentes werden mit den Ergebnissen aller analysieren Texte verglichen.

# ProfNet PlagiatService - Ergebnis Textvergleich (alle Vergleiche)



| Kriterium | Dimension | Prüfdokument | Erstprüfer | Fachbereich | Hochschule | Fachrichtung | Hausarbeiten | Seminararbeiten | Bachelor Thesen | Diplomarbeiten | Master Thesen | Dissertationen | Habilitationen | alle |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dokumente | Anzahl | 1 | 0 | 14 | 1 | 1302 | 73 | 39 | 350 | 2351 | 258 | 21741 | 176 | 41836 |
| Mischpl.-eine | Anzahl (Durchschnitt) | 0 | 0 | 2 | 0 | 1 | 1 | 6 | 1 | 1 | 1 | 3 | 3 | 3 |
| Teilplagiat | Anzahl (Durchschnitt) | 7 | 0 | 6 | 1 | 10 | 6 | 8 | 9 | 11 | 12 | 24 | 23 | 21 |
| Mischpl.-mehrere | Anzahl (Durchschnitt) | 0 | 0 | 1 | 0 | 2 | 2 | 2 | 2 | 3 | 3 | 6 | 4 | 5 |
| Zitierungsfehler | Anzahl (Durchschnitt) | 1 | 0 | 2 | 0 | 2 | 1 | 7 | 3 | 3 | 3 | 4 | 6 | 3 |
| Bauernopfer | Anzahl (Durchschnitt) | 16 | 0 | 1 | 0 | 4 | 1 | 0 | 2 | 2 | 3 | 3 | 3 | 3 |

● **39%** Gesamtplagiatswahrscheinlichkeit

Die Textvergleichsergebnisse des Prüfdokumentes werden mit allen analysierten Texten verglichen. Die Plagiatswahrscheinlichkeit wird grob vom Programm automatisch berechnet.

## Textstelle (Prüfdokument) S. 1

has been used as a forensic marker because it even at Vergewaltigungsopremotely by vasectomized men or azoospermische the safe detection of Semen allowed (SENSABOUGH and CRIM, 1978). Wang et al isolated and characterized from prostate tissues PSA (Wang et al., 1979). PAPSIDERO et al. showed PSA in serum only in patients with at advanced NEN prostate cancer according to (PAPSIDERO et al., 1980); however the home side's demand do not know in male and female control subjects. The authors concluded

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

bei Vergewaltigungsopfern durch vasektomierte oder azoospermische Männer den sicheren Nachweis von Samenflüssigkeit erlaubte (SENSABOUGH und CRIM, 1978). WANG und Mitarbeiter isolierten und charakterisierten PSA aus Prostatagewebe (WANG et al., 1979). PAPSIDERO et al. wiesen PSA im Serum nur bei Patienten mit einem fortgeschrittenen Prostatakarzinom nach ( PAPSIDERO et al., 1980); dagegen gelang der Nachweis bei männlichen und weiblichen Kontrollpersonen nicht.

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 1

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## Textstelle (Prüfdokument) S. 2

disease is and 1992 in the United States 132,000 Men suffering from this disease, is the differentiation between a particular nignen prostatic hyperplasia or prostate cancer a major challenge tion (BORING et al., 1993). 1.4. PSA Screening and With nearly 45% of patients with benign prostatic hyperplasia found diagnostic of the so-called "- a PSA increase from 4.0 to 10.0 ng /ml Gray zone". Since half of all 60-year-old men already a benign Prostatahy- exhibit hyperplasia, this means that almost every second patient in the urological Age of about 60 years, has a low increase in PSA (HAMMERER et al., 1992 Osterling, 1991).

● **1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

• **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5

## Textstelle (Prüfdokument) S. 2

Screening studies on 1653 and later to more than 10,000 men have each but found that not 50% but only 10% of all asymptomatic men in comprise the age group from 50 years a PSA level of> 4.0 ng / ml (Andriole and Catalona, a <a < 1993; Catalona et al., 1991; Catalona et al., 1993). These men with PSA values a <a <in the "gray zone" (4- by biopsy in 22% secured a prostate cancer to 27%. Lag the PSA level> 10 ng / ml, as found even in 59% to 67% a carcinoma. 4 In the international urological society is generally

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Männern haben jedoch gezeigt, daß nicht 50%, sondern nur 10% aller asymptomatischen Männer in der Altersgruppe ab 50 Jahren einen PSA-Wert von >4,0 ng/ml aufweisen (ANDRIOLE und CATALONA, 1993; CATALONA et al., 1991; CATALONA et al., 1993). Bei diesen Männern mit PSA-Werten in der "Grauzone" (4-10 ng/ml) wurde mittels Biopsie in 22% bis 27% ein Prostatakarzinom gesichert. Lag der PSA-Wert >10 ng/ml,

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 3

## Textstelle (Prüfdokument) S. 4

PSA levels increase the sensitivity in younger patients, the very likely to benefit from aggressive therapy and reduce by ERincrease the specificity, the biopsy rate of older men who no patients for these Therapy are (EL GALLEY et al., 1995). 2. PSA density (PSAD): The PSAD is the quotient of PSA and transrectal ultrasound-value prostate specific defined volume and is intended to improve the discriminant discrimination between benign prostatic hyperplasia and prostate cancer in invasive clinically relevant PSA

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

sehr wahrscheinlich von einer aggressiven Therapie profitieren und vermindern durch Erhöhung der Spezifität die Biopsie-Rate älterer Männer, die keine Patienten für diese Therapieform sind (EL-GALLEY et al., 1995). 2. PSA-Density (PSAD): Die PSAD ist durch den Quotienten aus PSA-Wert und transrektal-sonographisch bestimmten Prostatavolumen definiert und soll zu einer Verbesserung der Diskriminierung zwischen benigner Prostatahyperplasie

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 5

## Textstelle (Prüfdokument) S. 5

increase under the above restrictions. 7 1.5. PSA and staging in prostate cancer Many large studies have demonstrated for prostate cancer, the PSA that Serum levels with increasing clinical stage, pathologic stage and Tumor volume correlated (Osterling et al, 1988;. PARTIN et al, 1990;. Stamey et al., 1987; Stamey and Kabalin, 1989). Nevertheless, PSA alone is not so special Fish that for the individual patient an accurate, sole Staginginformation provides (Noldus and Stamey, 1996). The accuracy of the staging may by Introducing preoperative variables such as

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

beim Prostatakarzinom Viele große Studien haben für das Prostatakarzinom zeigen können, daß der PSA- Serumspiegel mit zunehmendem klinischen Stadium, pathologischen Stadium und Tumorvolumen korreliert (OESTERLING et al., 1988; PARTIN et al., 1990; STAMEY et al., 1987; STAMEY und KABALIN, 1989). Trotzdem ist PSA allein nicht so spezifisch, daß es für den individuellen Patienten eine akkurate, alleinige Staginginformation liefert ( NOLDUS und STAMEY, 1996). Die Genauigkeit

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 7

# Textstelle (Prüfdokument) S. 6

in theory at a benign ERdisease in other concentrations than are present in prostate cancer could and therefore could increase the specificity of PSA? PSA is specific to primates and is used in men almost exclusively by the Epithelial cells of the prostate gland androgen produced and secreted (MONTGOMERY et al. , 1992; NEAL et al., 1992). Typically, PSA is in Eja- Kulat in concentrations of 0.5 to 5.0 mg / ml (SENSABOUGH and CRIM, 1978); In contrast, the serum PSA concentration exceeds in healthy men, Patients with benign prostatic hyperplasia and usually in patients with prostate cancer a few nanograms per milliliters. Only a few patient can duck with advanced or metastatic prostate cancer predominantly NEN develop serum PSA values a <a <of several thousand nanograms per milliliter. Thus,

● **3%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

et al., 1988). Both the PA and hGK-1 gene are completely sequenced, their mutual homology is 82% (Schedlich et al., 1987; Riegman et al., 1989). PA is exclusively synthesized by the epithelial cells of the prostate gland (Wang et al. 1979,1981; Watt et al., 1986; Gallee et al., 1986). Its presumed function is dissolving the seminal coagulum by digesting proteins secreted by the seminal vesicles,

Spezifität des PSA erhöhen könnten? PSA ist spezifisch für Primaten und wird bei Männern fast ausschließlich von den Epithelzellen der Prostatadrüsen androgenabhängig produziert und sezerniert (MONTGOMERY et al., 1992; NEAL et al., 1992). Typischerweise liegt PSA im Ejakulat in Konzentrationen von 0,5 bis 5,0 mg/ml vor (SENSABOUGH und CRIM, 1978); dagegen übersteigt die Serum-PSA-Konzentration bei gesunden Männern, Patienten

from breast cyst fluids and 6 from amniotic fluids) with PSA levels higher than 0.2 pg/L, we measured free PSA levels (fPSA). We also measured P S A serum levels in 10 healthy men, 10 patients with benign prostatic hyperplasia (BPH) and 10 patients with prostate cancer. PSA was measured by an ultrasensitive fluoroimmunometric DELFIA assay (Prostatus PSA EQM, Wallac, Turku, Finland) based on the direct

- **3** Riegman, Pieter: Prostate-specific ..., 1992, S. 66
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 8
- **4** Filella, Xavier/u.a.: Detection of ..., 1996, S. 68

## Textstelle (Prüfdokument) S. 6

recently on Massenspektroskopie was determined (BELANGER et al., 1995). The by mass spectroscopy and Calculation based on the amino acid sequence ( about 33 kDa) different molecular Large weight is explained by an oligosaccharide at asparagine in position 45 (VAN HALBEEK et al., 1985). PSA still belongs to the family of serine proteases (WATT et al., 1986). Ten cystine in PSA correspond with likely Chymotrypsin, another serine protease and are probably due to the inactivation the PSA participated (Lundwall and LILJA, 1987).

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

wurde (BELANGER et al., 1995). Das durch Massenspektroskopie und Errechnung anhand der Aminosäurensequenz (ca. 33kDa) unterschiedliche Molekulargewicht wird durch eine Oligosaccharidkette am Aspargin in Position 45 erklärt (VAN HALBEEK et al., 1985). PSA gehört weiterhin zur Familie der Serin-Proteasen (WATT et al., 1986). Zehn Cystinreste im PSA korrespondieren wahrscheinlich mit Chymotrypsin, einerweiteren Serinprotease und sind vermutlich an der

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 9

## Textstelle (Prüfdokument) S. 8

permanently in slightly acidic medium of the vacuum ginalflAHssigkeit by the protease Gastriesin (SzA csi and LILJA, 1993). So far it has not been possible to isolate from serum PSA and the molecular structure to characterize. 12 Met-Trp-Val-Pro-Val-Val-Phe-Leu-Thr-Leu-Ser-Val-Thr-Trp-Ile Gly-Ala-7 Ala-Pro-Leu-Ile-Leu-Ser-Arg 1 Ile-Val-Gly-Gly-Trp-Glu-Cys-Glu-Lys-His-Ser-Gln-Pro-Trp-Gln Val-Leu-Val-Ala-Ser-Arg-Gly-Arg-Ala-Val-Cys-Gly-Gly-Val-Leu-Val-His-Pro-Gln-Trp-Val-Leu-Thr-Ala-Ala-His-Cys-Ile-Arg-Asn Lys-Ser-Val-Ile-Leu-Leu-Gly-Arg-His-Ser-Leu-Phe-His-Pro-Glu- Asp-Thr-Gly-Gln-Val-Phe-Gln-Val-Ser-His-Ser-Phe-Pro-His-Pro- Leu-Tyr-Asp-Met-Ser-Leu-Leu-Lys-Asn-Arg-Phe-Leu-Arg-Pro-Gly Asp-Asp-Ser-Ser-His-Asp-Leu-Met-Leu-Leu-Arg-Leu-Ser-Glu-Pro Ala-Glu-Leu-Thr-Asp-Ala-Val-Lys-Val-Met-Asp-Leu-Pro-Thr-Gln Glu-Pro-Ala-Leu-Gly-Thr-Thr-Tyr-Cys-Ala-Ser-Gly-Trp-Gly-Ser-Ile- Glu-Pro-Glu-Glu-Phe-Leu-Thr-Pro-Lys-Lys-Leu-Gln-Cys-Val-Asp- Leu-His-Val-Ile-Ser-Asn-Val-Asp-Cys-Ala-Gln-Val-His-Pro-Gln-Lys Val-Thr-Lys-Phe-Met-Leu-Cys-Ala-Gly-Arg-Trp-Thr-Gly-Gly-Lys Ser-Thr-Cys-Ser-Gly-Asp-Ser-Gly-Gly-Pro-Leu-Val-Cys-Asn-Gly- Val-Leu-Gln-Gly-Ile-Thr-Ser-Trp-Gly-Ser-Glu-Pro-Cys-Ala-Leu-Pro Glu-Arg-Pro-Ser-Leu-Tyr-Thr-Lys-Val-Val-His-Tyr-Arg-Lys-Trp-Ile Lys-Asp-Thr-Ile-Val-Ala-Asn-Pro 237 Figure 1: Amino acids sequence (AS) of the PSA molecule. Position -24 to -1: suspected AS-sequence (RIEGMANN et al., 1989). Position 1-237 AS-known sequence of the ejaculate (Schaller et al., 1987). 13 Figure 2: Tetrameric structure of the protease inhibitor a-2-macroglobulin (1)

**42%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

der Vaginalflüssigkeit durch die Protease Gastriesin (SZECSI und LILJA, 1993). Bisher ist es nicht gelungen, PSA aus Serum zu isolieren und die molekulare Struktur zu charakterisieren. Met-Trp-Val-Pro-Val-Val-Phe-Leu-Thr-Leu-Ser-Val-Thr-Trp-Ile- Gly-Ala-7 Ala-Pro-Leu-Ile-Leu-Ser-Arg- 1 Ile-Val-Gly-Gly-Trp-Glu-Cys-Glu-Lys-His-Ser-Gln-Pro-Trp-Gln- Val-Leu-Val-Ala-Ser-Arg-Gly-Arg-Ala-Val-Cys-Gly-Gly-Val-Leu- Val-His-Pro-Gln-Trp-Val-Leu-Thr-Ala-Ala-His-Cys-Ile-Arg-Asn- Lys-Ser-Val-Ile-Leu-Leu-Gly-Arg-His-Ser-Leu-Phe-His-Pro-Glu- Asp-Thr-Gly-Gln-Val-Phe-Gln-Val-Ser-His-Ser-Phe-Pro-His-Pro- Leu-Tyr-Asp-Met-Ser-Leu-Leu-Lys-Asn-Arg-Phe-Leu-Arg-Pro-Gly- Asp-Asp-Ser-Ser-His-Asp-Leu-Met-Leu-Leu-Arg-Leu-Ser-Glu-Pro- Ala-Glu-Leu-Thr-Asp-Ala-Val-Lys-Val-Met-Asp-Leu-Pro-Thr-Gln- Glu-Pro-Ala-Leu-Gly-Thr-Thr-Cys-Tyr-Ala-Ser-Gly-Trp-Gly-Ser-Ile- Glu-Pro-Glu-Glu-Phe-Leu-Thr-Pro-Lys-Lys-Leu-Gln-Cys-Val-Asp- Leu-His-Val-Ile-Ser-Asn-Asp-Val-Cys-Ala-Gln-Val-His-Pro-Gln-Lys Val-Thr-Lys-Phe-Met-Leu-Cys-Ala-Gly-Arg-Trp-Thr-Gly-Gly-Lys- Ser-Thr-Cys-Ser-Gly-Asp-Ser-Gly-Gly-Pro-Leu-Val-Cys-Asn-Gly- Val-Leu-Gln-Gly-Ile-Thr-Ser-Trp-Gly-Ser-Glu-Pro-Cys-Ala-Leu-Pro Glu-Arg-Pro-Ser-Leu-Tyr-Thr-Lys-Val-Val-His-Tyr-Arg-Lys-Trp-Ile- Lys-Asp-Thr-Ile-Val-Ala-Asn-Pro 237 Abbildung 1: Aminosäuren-Sequenz (AS) des PSA-Moleküls. Position -24 bis -1: vermutete AS-Sequenz (RIEGMANN et al., 1989). Position 1 bis 237 bekannte AS-Sequenz aus Ejakulat (SCHALLER et al., 1987).

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 12

## Textstelle (Prüfdokument) S. 9

prostatic hyperplasia? 2. Is there a "cut-off" value of the percentage free PSA for prostate cancer? 3. Influences of BPH prostate share reflects the percentage of free PSA? 4. Does the determination of free PSA in the serum in the staging of localized Prostate cancer? PAPSIDERO and co-workers showed in 1980 that PSA in the serum in two molecules secular forms, a 100,000 kDa and 34, 000 kDa form is present (PAPSIDERO et al., 1980). 1990 reported LILJA and STENMAN according independently, that PSA predominantly bound

● **1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

in a community-based population of healthy men: Establishment of age-sp.? cific reference ranges. 270:860, 1993 33. Partin AW, Carter HB, Chan DW, et al: Prostate specific antigen in the staging of localized prostate cancer: Influence of tumor differentiation, tumor volume and benign hyperplasia. J Urol 143:747,1990 34. Riehmann M, Rhodes PR, Cook TD, et al: Analysis of variation in prostate-specific antigen values.

• **5** Oesterling, J.E./Cooner, W.H., Jaco..., 1993, S. 680

# Textstelle (Prüfdokument) S. 9

kDa and 34,000 kDa form is present (PAPSIDERO et al., 1980). 1990 reported LILJA and STENMAN according independently, that PSA predominantly bound in the serum to the protease inhibitor ACT and not in free, unbound form is present (LILJA et al., 1991;. STENMAN et al, 1991). Furthermore made STENMAN et al. the observation that PSA complexed to ACT present in patients with benign prostatic hyperplasia in lower percentage is as in patients with untreated prostate cancer (STENMAN et al., 1991). Conversely could Christensson et al. show that the proportion of free, not to a protease inhibitor bound PSA in patients with untreated

**2%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

al., 1980). 1990 wiesen LILJA und STENMAN unabhängig voneinander nach, daß PSA im Serum überwiegend an den Proteaseninhibitor ACT gebunden und nicht in freier, ungebundener Form vorliegt (LILJA et al., 1991; STENMAN et al., 1991). Weiterhin machten STENMAN et al. die Beobachtung, daß PSA komplexiert an ACT bei Patienten mit einer benignen Prostatahyperplasie in niedrigerem Prozentsatz vorliegt als bei Patienten

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 14
- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5

## Textstelle (Prüfdokument) S. 9

patients with untreated prostate cancer (STENMAN et al., 1991). Conversely could Christensson et al. show that the proportion of free, not to a protease inhibitor bound PSA in patients with untreated Prostate cancer was significantly lower (18%) "as in patients with a benign Prostatic hyperplasia (28%) and that the ratio of free PSA share regardless dependent on the level of total serum PSA concentration (Christensson et al., 1993). It was concluded that, by the determination of free PSA the discrimination between patients with benign prostatic hyperplasia and prostate cancer could be facilitated. Stamey and employees were show on pooled sera from patients with prostate cancer that the pro- centage ratio of PSA-ACT regardless of complexation to Tumorvolu- 15 men, the clinical stage and the

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

ultrasound. Baltimore, American Urological Association 1992 Policy Statement Book, 1992, p 4.20 2- Armitage TG, Cooper EH, Newling WW, et al : The value of the measurement of serum prostate specific antigen in patients with benign prostatic hyperplasia and untreated prostate cancer. Br J Urol 62: 584, 1988 3- Benson MC, Whang IS, Olsson CA, et al: The use of prostate specific antigen density to enhance the predictive value

PSA. ClinChem 1994; 40:1009. 18. King C, Friese J, Lauren L, Dowell B, Shaw N, Lilja H, et al. Measurement on IMx of free and total forms of prostate-specific antigen for differentiation of patients with benign prostatic hyperplasia and prostate cancer. Clin Chem 1994; 40:1007. 19. Dowell B, King C, Weatherholt J, Schaefer V. Differential recognition of PSA forms is not reflected in the clinical performance of IMx PSA. Presented at XXII Meeting of

- **5** Oesterling, J.E./Cooner, W.H., Jaco..., 1993, S. 679
- **6** Gottschling, Hans-Detlef/et al.: Mu..., 1995, S. 392

## Textstelle (Prüfdokument) S. 10

showed that patients where the growth of tumors receiving hormonal therapy or after radiation therapy was progressive, the same sequestering proportion had (Stamey et al., 1994). So far, all these issues raised were only partially examined (LILJA et al., 1991; . Stamey et al, 1994; STENMAN et al., 1991). The first is by collectives with relatively small numbers of patients, on the other hand is not ex- Act histological diagnosis before. Histological diagnosis is but important inasmuch as in the relevant age group, the prevalence of Prostate cancer is at least 40%. Furthermore, no data exist in the Literature whether

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

ungebundenen und der an a-1-Antichymotrypsin gebundenen Form. Da bekannt ist, daß die freie Fraktion des PSA bei Patienten mit einem Prostatakarzinom nur ca. 5 bis 15% beträgt (LILJA et al., 1991; STAMEY et al., 1994; STENMAN et al., 1991), war es notwendig, Sera mit sehr hohen Gesamt-PSA-Werten zu verwenden. Dieses liegt in der Regel bei Patienten mit metastasierten, unbehandelten oder therapierefraktären Prostatakarzinomen

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 68

# Textstelle (Prüfdokument) S. 10

The present study investigated this question for the first time at the biggest group of patients with histologically safer definition. IIb. For the clinical part: 1. Improves the provision of additional serum parameters testosterone, Dihydrotestosterone (DHT), luteinizing hormone (LH) and follicular stimulating hormone (FSH), the diagnostic accuracy a) the differentiation between prostate cancer at and a benign prostatic hyperplasia? b) in the staging of localized prostate cancer? 16 The growth and development of the prostate is an androgen-dependent process process, which already WHITE and CABOT discovered end of last century (Cabot, 1896; WHITE, 1893). Huggins and co-workers used this effect to Treatment of advanced prostate cancer in [1941] ( Huggins et al., Testosterone reduced (Shapiro, 1990). Consequently, it is believed that the formation of PSA also runs androgen through the epithelial cell of the prostate (MONTGOMERY et al., 1992; NEAL et al., 1992). The surgical or medication thera- castration usually leads to a significant reduction in the serum PSA level, which in patients with prostate cancer receiving hormonal or so-called anti-androgenic therapy can be well observed. On the other hand the supply of exogenous testosterone the PSA level can the older man increase (Tenover, 1992). It was therefore obvious that influence of testosterone, DHT, LH and FSH on the developdevelopment

**4%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

behavior are transformed into neuroendocrine responses. Gonatrophin releasing factor (GRF) is released from the hypothalamus irregularly in bursts. The ante rio-pituitary in response releases luteinizing hormone (LH) and follicular stimulating hormone (FSH), also in episodic bursts of secretion. In the normal male, FSH acts on the germinal epithelium of the seminiferous tubules to produce spermatazoa. LH stimulates

in a community-based population of healthy men: Establishment of age-sp.? cific reference ranges. 270:860, 1993 33. Partin AW, Carter HB, Chan DW, et al: Prostate specific antigen in the staging of localized prostate cancer: Influence of tumor differentiation, tumor volume and benign hyperplasia. J Urol 143:747,1990 34. Riehmann M, Rhodes PR, Cook TD, et al: Analysis of variation in prostate-specific antigen values.

of the epithelial cell layers and in the morphogenesis of the prostate (Chung & Cunha, 1983; Tenniswood, 1986; Cunha et al., 1987; Chang & Chung, 1989; Chung et al., 1990). The normal growth and development of the prostate is strongly androgen dependent. Androgen action is mediated by the androgen receptor (AR) in target cells (discussed more extensively in 1.3). The AR is a ligand-responsive transcription

Holdaway IM, Haefliger J-M, Jordaan JP, and Sotarauta M:A multicenter randomized trial comparing the luteinizing hormone-releasing hormone analogue oserelin acetate alone and with flutamide in the treatment of advanced prostate cancer. Th International Prostate Cancer Study Group. J Urol 146: 1321-1326, 1991. 8. Brandt B, Menu G, E1Khansa A,and Lardenois B:Monitoring of prostate volume by ultrasound in hormonally treated prostate cancer. Prog Clin

Spezifität des PSA erhöhen könnten? PSA ist spezifisch für Primaten und wird bei Männern fast ausschließlich von den Epithelzellen der Prostatadrüsen androgenabhängig produziert und sezerniert (MONTGOMERY et al., 1992; NEAL et al., 1992). Typischerweise liegt PSA im Ejakulat in Konzentrationen von 0,5 bis 5,0 mg/ml vor (SENSABOUGH und CRIM, 1978); dagegen übersteigt die Serum-PSA-Konzentration bei gesunden Männern, Patienten

- **7** Bradford, John: The hormonal treatm..., 1983, S.
- **5** Oesterling, J.E./Cooner, W.H., Jaco..., 1993, S. 680
- **3** Riegman, Pieter: Prostate-specific ..., 1992, S. 5
- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 1987
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 8

## Textstelle (Prüfdokument) S. 11

of benign prostatic hyperplasia and prostate cancer terms an improved PSA specificity investigate. This question is indeed other sets have already been examined by employees of the Mayo Clinic (MONDA et al., 1995), but never on a large enough group of patients with histologisch

1941). Androgen is today still a common treatment option in the

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

as a serum marker for adenocarcinoma of the prostate. N Engl J Med 317: 909 28. Lee F. Littrup P. Loft-Christcnsen L (1992) Predicted prostate specific antigen results using transrectal ultrasound gland volume; differentiation of benign prostatic hyperplasia and prostate cancer. Cancer 70: 211-220 29. Oesterling JE. Chan DW. Epstein JI (1988) Prostate-specific antigen in the preoperative and postoperative evaluation of localized prostatic cancer treated with radical prostatectomy. J Urol 139: 766-771 30.

- **8** Hilz, H.: Molekulare Formen des PSA..., 1995, S. 282

## Textstelle (Prüfdokument) S. 11

on a large enough group of patients with histologisch through multiple prostate biopsies confirmed diagnosis. 17 3. Material and methods 3.1. EXPERIMENTAL SECTION Molecular characterization of free PSA (f-PSA) 3.1.1. The serum of patients with prostate cancer Were chosen from 59 patients with metastatic prostate cancer sera. These were the Department of Urology at Stanford University, CA, USA at -70 A C. stored. Due to the known low percentage proportion of free PSA in Serum (approximately 5% to 15%) were chosen such Sera whose total PSA

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Flutamide + bilateral orchiectomy 9 29 [71] .5 Flutamide + leuprolide 4 13 Total 31 1 O0 procedures and radiation or hormonal therapy. In 1989, Stamey et al. 6 reported a mean net-PSA decrease of 95% in previously untreated patients with metastatic prostate cancer disease undergoing hormonal therapy. It is also well known that the prostate size decreases during androgen suppression, 2,3,7 a finding usually confirmed by digital rectal examination. However,

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 31

## Textstelle (Prüfdokument) S. 11

in 23 different, successive runs An 10 ml fractionated. There was a Sephacryl S-200 column (2.5 x 92 cm) was used with a 20 mM sodium phosphate buffer (pH 7.4; 0.15 M sodium chloride) was equilibrated. The S-200 column was washed with the molecular weight markers Dextran blue (200 kDa) Albumin (67 kDa), chymotrypsin A (25 kDa) and ribonuclease A (13.7 kDa) Potash brated. The column flow-through fractions were 90 A§ 4 ml at a FluAYgeschwindigspeed of 0.35 ml / min fractionated. In order to keep the protein losses low, were silicon konisierte vials used. Between runs, the column

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

eine Sephacryl S-200 Säule (2,5 x 92 cm) verwendet, die mit einem 20 mMol Natriumphosphat-Puffer (pH 7,4; 0,15 Mol Natriumchlorid) äquilibriert wurde. Die S-200 Säule wurde mit den Molekulargewicht-Markern Dextran blau (200 kDa), Albumin (67 kDa), Chymotrypsin A (25 kDa) und Ribonuklease A (13,7 kDa) kalibriert. Je Säulendurchlauf wurden 90 Fraktionen ä 4 ml bei einer Flußgeschwindigkeit von 0,35 ml/min fraktioniert. Um den Proteinverlust gering zu halten, wurden silikonisierte Probengläser

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 17

## Textstelle (Prüfdokument) S. 12

case washed over at least 72 hours with the above buffer solution. 3.1.3. Immuno assay and spectrophotometry All PSA determinations both from serum and from the gel chromatographically separated fractions were done using the TOSOH AIAA -6 0 0 Immunoassay (TOSOH Medics, Foster City, CA, USA), an automated assay with a monoclonal antibody. As PSA standard value, a reference area specified from 0-4.0 ng / ml. All fractions of the free, unbound PSA were collected and spectrophotometers photometrically examined at a wavelength of 280 nm (A28O). In

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

gewaschen. 3.1.3. Immun-Assay und Spektrophotometrie Sämtliche PSA-Bestimmungen sowohl aus Serum als auch aus den gelchromatographisch aufgetrennten Fraktionen erfolgten mit dem TOSOH AIA -600 Immun-Assay ( TOSOH Medics, Foster City, CA, U.S.A.), ein automatisierter Assay mit einem monoklonalen Antikörper. Als PSA-Normwert wird ein Referenzbereich von 0-4,0 ng/ml angegeben. Alle Fraktionen des freien, ungebundenen PSA wurden gesammelt

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 18

## Textstelle (Prüfdokument) S. 12

automated assay with a monoclonal antibody. As PSA standard value, a reference area specified from 0-4.0 ng / ml. All fractions of the free, unbound PSA were collected and spectrophotometers photometrically examined at a wavelength of 280 nm (A28O). In all 23 runs the fractions with the highest specific activity (PSA (ng / ml) / A280) pooled and concentrated by an Amicon PM 10 filter (Amicon, Beverly, MA, USA) concentered. All 23 thus obtained samples of free PSA were again pooled and concentrated by the filter above. 3.1.4. Gel chromatography II For

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

very misleading, especially when presented graphically against a scale other than the relative protein content of the fractions. The suggestion that there is more enzyme in the fractions with the highest specific activity is very strong, obscuring the fact that the fractions concerned could contain only small amounts of protein and little enzyme activity. Similarly, the absence of

- **9** de Duve, Christian: Tissue fraction..., 1971, S. 74

## Textstelle (Prüfdokument) S. 12

pooled and again by the filter above concentrated. 19 3.1.5. Electrophoresis and Western blot technique, To keep the loss of free PSA low, carried the further separation of Proteins by electrophoresis. Was elected the sodium dodecyl sulfate Polyacrylamide gel electrophoresis (SDS-PAGE) according to the method of Laemmli (Laemmli, 1970) with modifications (Schagger and von Jagow, 1987). It were Mini gels (Bio Rad Mini-Protein II) having the dimensions 8.0 cm x 7.3 cm other manufactured. Table 2 and Table 3 show the gel compositions and use Deten buffer solutions.

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

were then heated at 50 C for 30 min before electrophoresis, care being taken not to evaporate the disulfide reducing agents . The samples were then analyzed by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) according to the method of Fairbanks, et al . (5), using 8% gels with 0.3% N, N'-methylenebisacrylamide. RESULTS AND DISCUSSION The bulk isolation procedure results in 1-5 mg (dry weight) of gap junctions . There is variability

- **10** Goodenough, Danial A.: BULK ISOLATI..., 1974, S.

# Textstelle (Prüfdokument) S. 13

with 30 volts carried out at room temperature; reached the proteins the separation gel (after about 45 min.), the voltage was increased to 90 volts. Table 2: electrophoresis gel composition Chemicals Separating gel j Collecting gel Soln. A A 3.33 mi 0.75 ml Soln. B + 2.0 ml J 0.2 5 ml Glycerol 1.33 g J dd H2 0 ad 10.0 ml i 3 . 5ml Ammonium persulfate 10% 33 uJ 15 uJ TEMED 3.3 uJ 1.5 uJ FMN * 100 | il A: 3.0 M Tris, 0.3% SDS + B: 48.0 g acrylamide, 1.5 g bisacrylamide ad 100ml ddH20 * FMN: Flavin mononucleotide 20 Table 3: Electrophoresis buffer solutions Anode buffer 0.2 M Tris, 350 ml Cathode buffer 2.68g Tricine 1.83 g Tris 0.15 g SDS dd H20 ad 150 ml After SDS-PAGE the proteins were both on a polyvinylidene difluoride Membrane (PVDF) (Bio-Rad Laboratories, Hercules, CA, USA) as well as on an Immobilized nitrocellulose membrane (Schleicher and Schuell, Keene, NH, USA) (MATSUDAIRA, 1987). Tables 4 and 5 show the transfer buffers used Solutions. Was transferred over 16 hours at 30 volts in the refrigerator (4 C). Table 4: Transfer buffer solution for PVDF membrane 10 mM CAPS (3- (cyclohexylamino) -1-propanesulfonic acid) 21 Table 5: Transfer buffer solution for

**6%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

das Trenn-Gel (nach ca. 45 min.), wurde die Spannung auf 90 Volt erhöht. Tabelle 2: Elektrophorese-Gel Zusammensetzung Chemikalien Trenn-Gel j Sammel-Gel Lsg. A 3,33 mi 0,75 ml Lsg. B+ 2,0 ml J 0,25 ml Glycerol 1,33 g J dd H20 ad 10,0 ml i 3,5 ml Amoniumpersulfat 10% 33 uJ 15 uJ TEMED 3,3 uJ 1,5 uJ FMN - 100 |il A: 3,0 M Tris, 0,3% SDS + B: 48,0g Acrylamid, 1,5g Bisacrylamid ad 100ml ddH20 * FMN: Flavin Mononucleotid Tabelle 3: Elektrophorese-Puffer Lösungen Anoden Puffer 0,2 M Tris, 350 ml Kathoden Puffer 2,68 g Tricine 1,83 g Tris 0,15 g SDS dd H20 ad 150 ml Nach der SDS-PAGE wurden die Proteine sowohl auf eine Polyvinylidendifluorid- Membran ( PVDF) (Bio-Rad Laboratories, Hercules, CA, U.S.A.) als auch auf eine Nitrozellulose-Membran (Schleicher und Schuell, Keene, NH, U.S.A.) immobilisiert (MATSUDAIRA, 1987). Tabellen 4 und 5 zeigen die verwendeten Transfer-Puffer Lösungen. Transferiert wurde über 16 Stunden

the connexin immunoblots. The protein samples were loaded on a 10% sodium dodecyl sulfate polyacrylamide gel. After electrophoresis at 50 mA [10] for 1. h, the proteins were transferred on to a nitrocellulose membrane (0.2 mm; Schleicher and Schuell, Keene, [10] NH, USA) at 200 mA for 1 h using a Semi-Dry Blotter [10] (Model IMM-1, WEP Co, Seattle, WA, USA) electrotransfer unit (transfer buffer: 12.5 mm Tris, pH 8.0, 96 mm [10] glycine, 10% methanol and 0.01% SDS ). The

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 19
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 20
- **11** Vrionis, FD/et al.: The bystander e..., 1997, S. #P10#Biol 1991; 3: 608 614. 58521

# Textstelle (Prüfdokument) S. 15

with the ER first mouse monoclonal antibody against PSA (F5, 1: 3000 in 0.1% BSAphosphate Buffer) for 1 hour followed by washing the membrane alternately TS (10 mM Tris; 0.1 M NaCl), TST (10 mM Tris; 0.1 M NaCl; 0.05% Tween Lane 2 insulated, free PSA of prostatic i nom serum (f-PSA, P-Ca) f-PSA, P-Ca 18u.l + SDS * buffer (4%) 3 | xl Bahn 3 insulated, free PSA of prostatic i nom serum (f-PSA, P-Ca) f-PSA, P-Ca 18u.l + |: ÄY-Mercaptoethanol SDS * buffer (5%) 3 A .1 Bahn 4 Control; free PSA from seminal fluid (f-PSA, SF) (Concentration 3.75 mg / ml., 1: 100) f-PSA, SF 4 | il + ddH20 8fil + SDS * -; Buffer (4%) 4u, l * SDS buffer: 4% (or 5%) SDS; 20% sucrose; 0.1 M Tris, pH 7.0; 0.1% Bromophenol Blue 23 Table 6b: composition of the samples for electrophoresis for later Transfer to nitrocellulose and PVDF membrane Bahn 1 Rainbow Marker (RM) RM 2,5u.l + ddH20 7,5jil + SDS * buffer (4%) 3UJ Lane 2 insulated, free PSA from prostate cancer serum (f-PSA, P-Ca) f-PSA, P-Ca 18jil + ÄY-mercaptoethanol SDS-* buffer (5%) 3 | XL Bahn 3 insulated, free PSA from prostate cancer serum (f-PSA, P Ca) f'-PSAE, P-Ca 18jlf + SDS * buffer (4%) 3jjlI Bahn 4 Control; free PSA from seminal fluid (f-PSA, SF) (Concentration 3.75 mg / ml., 1: 100) f'-PSAE, SF 4p + ddH20 8 | llI + S'Ä-S * buffer (4%) 4 | il ISDS buffer: .4% (bzw._5%) SDS; 20% sucrose; 0.1 MTris, pH 7.0; 0.1% Bromophenol Blue 24 For staining of the protein bands, the gels with Coomassie Brilliant Blue R-250 were (0.1% in 50% methanol) colored. The stained gels were in 5% glycerol solution conserved. The

**8%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

Proben für die Elektrophorese zur Färbung mit Coomassie Brilliantblau R-250 Bahn 1 MW 2uJ + dd H20 6jil + SDS*-Puffer Molekulargewicht-Marker ( MW) (4%) 3uJ Bahn 2 isoliertes, freies PSA aus Prostatakarzi- i nom-Serum (f-PSA, P-Ca) f-PSA, P-Ca 18u.l + SDS*-Puffer (4%) 3|xl Bahn 3 isoliertes, freies PSA aus Prostatakarzi- i nom-Serum (f-PSA, P-Ca) f-PSA, P-Ca 18u.l + :ß-Mercaptoethanol-SDS*-Puffer (5%) 3 .1 Bahn 4 Kontrolle; freies PSA aus Samenflüssigkeit (f-PSA, SF), (Konz. 3,75 mg/ml,1:100) f-PSA, SF 4|il + ddH20 8fil + SDS*-; Puffer (4%) 4u,l * SDS-Puffer: 4% (bzw. 5%) SDS; 20% Saccharose; 0,1 M Tris, pH 7,0; 0,1% Bromophenol Blau Tabelle 6 b: Zusammensetzung der Proben für die Elektrophorese zum späteren Transfer auf Nitrozellulose und PVDF Membran Bahn 1 Regenbogen-Marker (RM) RM 2,5u.l + ddH20 7,5jil + SDS*-Puffer (4%) 3uJ Bahn 2 isoliertes, freies PSA aus Prostatakarzinom-Serum (f-PSA, P-Ca) f-PSA, P-Ca 18jil + ß-Mercaptoethanol-SDS*-Puffer(5%) 3|xl Bahn 3 isoliertes, freies PSA aus Prostatakarzinom-Serum (f-PSA, P-Ca) f'-PSÄ, P-Ca 18jlf + SDS*-Puffer (4%) 3jjlI Bahn 4 Kontrolle; freies PSA aus Samenflüssigkeit (f-PSA, SF), (Konz. 3, 75 mg/ml, 1:100) f'-PSÄ, SF 4p + ddH20 8|llI + S'ÖS*-Puffer (4%) 4|il ISDS -Puffer: .4% (bzw._5%)SDS; 20% Saccharose; 0,1 MTris, pH7,0; 0,1% Bromophenol Blau Zur Färbung der Proteinbanden wurden die Gele mit Coomassie Brillantblau R-250 (0,1% in 50% Methanol) gefärbt. Die

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 22
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 23

## Textstelle (Prüfdokument) S. 17

only the PSA recognizes that is not complexed to ACT. The working range of the assay is between 0.1 and 100 ng / ml. The entire analysis process was carried out of all samples fully automatically by the Immulite Automated Analyzer (IMMULITE MANUAL, 1995). The percentage of the f-PSA to the PSA was on the t-formula (f-PSA / t- PSA) * 100% charged. In the Department of Clinical Chemistry II. Medical Clinic of the University Hospital Hamburg-Eppendorf (Head: Prof. Dr. C. Wagener) were of 148

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

erkennt, welches nicht an ACT komplexiert ist. Der Arbeitsbereich des Assays liegt zwischen 0,1 und 100 ng/ml. Der gesamte Analysevorgang aller Proben erfolgte vollautomatisch durch den Immulite Automated Analyzer (IMMULITE MANUAL, 1995). Der prozentuale Anteil des f-PSA am t-PSA wurde über die Formel (f-PSA/t- PSA)*100% berechnet. In der Abteilung für Klinische Chemie der II. Medizinischen Klinik des Universitäts-

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 27

## Textstelle (Prüfdokument) S. 18

patients was additionally the dihydrotestosterone (DHT) determined (Standard value DHT: 35.7 to 573 pg / ml). LH and FTH (Bayer Diagnostics, Munich) were the means of an enzyme-linked immunosorbent assays, testosterone ( Biermann GmbH, Bad Nauheim home) and DHT (Diagnostics Systems Laboratories, Sinsheim) by means of a solid phase sen radioimmunoassay assays determined. All samples were taken also against any Prostate manipulation. 3.2.4. Statistical Methods As statistical tests of Mann-Whitney U and Kruskal-Wallis test for were Comparing two or

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Dihydrotestosteron (DHT) bestimmt (Normwert DHT: 35,7-573 pg/ml). LH und FTH (Bayer Diagnostics, München) wurden mittels eines Enzym-Immun-Assays, Testosteron (Biermann GmbH, Bad Nauheim) und DHT (Diagnostics Systems Laboratories, Sinsheim) mittels eines Festphasen- Radioimmun-Assays bestimmt. Alle Abnahmen erfolgten ebenfalls vor jeglicher Prostatamanipulation. 3.2.4. Statistische Methoden Als statistische Tests wurden der Mann-Whitney-U- und Kruskal-Wallis-

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 28

## Textstelle (Prüfdokument) S. 19

value X" a '<' - sign occurs because a lower f-PSA% value for the existence of a prostatakarzinoms speaks. The statistical calculations were in cooperation with Dipl. Math. Dr. C. Busch performed. 4. Results 30 4.1. EXPERIMENTAL SECTION 4.1.1. Isolation of free PSA 230 ml serum from 59 patients with metastatic prostate cancer were in 23 individual gel chromatographic runs separated. The computational PSA Total-immune activity was 480,000 ng. Representative of all 23 runs shows Figure 3 clearly the high and broad protein peak fraction between 33 to 64. shows the determination of

● **1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Flutamide + bilateral orchiectomy 9 29 [71] .5 Flutamide + leuprolide 4 13 Total 31 1 O0 procedures and radiation or hormonal therapy. In 1989, Stamey et al. 6 reported a mean net-PSA decrease of 95% in previously untreated patients with metastatic prostate cancer disease undergoing hormonal therapy. It is also well known that the prostate size decreases during androgen suppression, 2,3,7 a finding usually confirmed by digital rectal examination. However,

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 31

## Textstelle (Prüfdokument) S. 20

collected Group with PSA-ACT peak between Group 40 and 60 and f-PSA Peak between Group 61 and 73rd 32 Number of fractions Figure 4: Gel chromatography II: significant protein peaks (A280) between the Fractions 19 and 29, and a flatter peak between fractions 33 800 - N (OO * 00N (0O * 00N (0O * 00N (0O TtT CM CM CO CD CO Tj Tj-IOLO LO CO CD h- Number of fractions Figure 5: PSA activities (ng / ml) of the fractions collected from gel chromatography II: PSA-ACT peak between fractions 12 and 20 and f-PSA summit between Fractions 34 and 50th 34 4.1.[2] . Electrophoresis and Western Blot By gel filtration

2) could not differentiate between these two bands. The F5 antibody

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Fraktion 40 und 60 sowie f-PSA Peak zwischen Fraktion 61 und 73. Anzahl der Fraktionen Abbildung 4: Gelchromatographie II: Deutlicher Proteingipfel ( A280) zwischen den Fraktionen 19 und 29 sowie flacherer Gipfel zwischen den Fraktionen 800 - N(OO*00N(0O*00N(0O*00N(0O T-t-T-CM CM CO CD CO Tj-Tj-IOLO LO CO CD h- Anzahl der Fraktionen Abbildung 5: PSA-Aktivitäten (ng/ml) der gesammelten Fraktionen aus Gelchromatographie II: PSA-ACT-Gipfel zwischen den Fraktionen 12 und 20 sowie f-PSA-Gipfel zwischen Fraktionen 34

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 33

## Textstelle (Prüfdokument) S. 21

of the PSA molecule (Schaller et al., 1987). 35 30 kDa Figure 6a: SDS-PAGE of the isolated f-PSA. Partially insulated f-PSA was measured by denaturing gel electrophoresis analyzed further. Lane 1: molecular weight markers ( phosphorylase B, 94kDa, ovalbumin, 43kDa; Carboniferous anhydrase, 30 kDa; Trypsin Inhibitor, 20 kDa) Lane 2: Partially f-PSA isolated from serum of patients with Prostate cancer Lane 3: Partially f-PSA isolated from serum of patients with Reduces prostate cancer sample with 1% beta-mercaptoethanol Lane 4: control, purified PSA from Ekakulat 36 30 kDa Figure 6b:

● **1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

ECL-Technik (Bahn Abbildung 6a: SDS-PAGE des isolierten f-PSA. Partiell isoliertes f-PSA wurde mittels denaturierender Gelelektrophorese weiter analysiert. Bahn 1: Molekulargewichtsmarker (Phosphorylase B, 94kDA; Ovalbumin, 43kDa; karbonische Anhydrase, 30kDa; Trypsin Inhibitor, 20kDa) Bahn 2: Partiell isoliertes f-PSA aus Serum von Patienten mit Prostatakarzinom Bahn 3: Partiell isoliertes f-PSA aus Serum von Patienten mit Prostatakarzinom, Probe mit 1% ß-Mercaptoethanol reduziert Abbildung 6b:

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 35

## Textstelle (Prüfdokument) S. 22

Lane 2: Partially f-PSA isolated from serum of patients with Reduces prostate cancer sample with 1% beta-mercaptoethanol Lane 3: Partially f-PSA isolated from serum of patients with Prostate cancer Lane 4: control, purified PSA from Ekakulat 37 Position 1 2 3 4 5 6 7 8 9 i 146 148 149 150 151 152 p; Ejaculate AS-Seq. Ile Val Gly Gly Trp Glu Cys Glu Lys 1 Lys Leu Gin Cys Val Asp Leu H PCa serum AS-Seq. Ile Val Gly Gly Trp Glu Cys Glu Lys 1 Lys Leu Gin Cys Val Asp Leu U CO Figure 7: Congruent amino acids (aa) sequence of the PSA molecule of ejaculate (Schaller et al., 1987) and from serum of Patients with prostate cancer (PCa). 38 4.2. Clinical part 4.2.1. Differentiation between prostate cancer and benign Prostatic hyperplasia 4.2.1.1. Age distribution

**7%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Partiell isoliertes f-PSA aus Serum von Patienten mit Prostatakarzinom, Probe mit 1% ß-Mercaptoethanol reduziert Bahn 3: Partiell isoliertes f-PSA aus Serum von Patienten mit Prostatakarzinom Position 1 2 3 4 5 6 7 8 9 i 146 147 148 149 150 151 152 p; Ejakulat AS-Seq. Ile Val Gly Gly Trp Glu Cys Glu Lys 1 Lys Leu Gin Cys Val Asp Leu H PCa-Serum AS-Seq. Ile Val Gly Gly Trp Glu Cys Glu Lys 1 Lys Leu Gin Cys Val Asp Leu U CO Abbildung 7: Übereinstimmende Aminosäuren (AS)-Sequenz des PSA-Moleküls aus Ejakulat (SCHALLER et al., 1987) und aus Serum von Patienten mit Prostatakarzinomen (PCa). 4.2. Klinischer Teil 4.2.1. Differenzierung zwischen

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 37

# Textstelle (Prüfdokument) S. 22

from serum of Patients with prostate cancer (PCa). 38 4.2. Clinical part 4.2.1. Differentiation between prostate cancer and benign Prostatic hyperplasia 4.2.1. 1. Age distribution Of 259 patients were able to prostate biopsies 148 patients ( 57.1%) with be diagnosed prostate cancer. The remaining of the 111 patients ( 42.9%) had no cancer, they were classified as patients with benign prostate tahyperplasie counted. The average age of patients with benign prostatic hyperplasia was 63 . 8 Years (range: 31-88 years), the patients with prostate cancer 65.1 years (Range: 45-88 years). Table 9 shows that the age section between 60 and 69 years Ren, the majority of patients with benign prostatic hyperplasia (50%) and prostate cancer (43.7%) were diagnosed. _ Table 9: Age distribution in patients with benign prostatic hyperplasia (n = 94) and prostate cancer (n = 142) Age (years) ] <40 40-49 50-59 60-69 | 70-79 j > 80 benign Prbstatahyp. i I! 114 (14.9) j n (%) ! 1 (1.1) 4 (4.3) 22 (23.4) 47 (50. 0) 6 (6.3) Prostat nkarzinom I I n (%) 0 5 (3.5) 35 (24.6) 1 62 (43.7) I 32 (22. 6) ! 8 (5.6) 39 4.2.1.2. Preoperative PSA levels Loading The average PSA level for all 148 patients with established prostate cancer 26.7 wore

**13%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

combination of an antiandrogen plus medical or surgical [18] castration. Their mean age was 71.5 years (range, [18] 53 to 82), with a mean follow-up of 29 months [18] (range, 12 to 41; median, 31). Of the 13 patients, [18] 8 (62%) had no failure; the remaining 5 men [18] (38%) showed disease progression at an average [71] 71 4 UROLOGY 47 (5), 1996 [6] 6 25 22.8 11 0.5 56 10 0.01 8 0.06 10 0.07 68 [7] 7 135 67.7 74 0.3 45.2 68 § 1.63 § 54 § 2.98 § 60 [8] 8 56 14.6 44 1.3 21.4 44 0.3 29 0.1 37 0.01 48.2 [9] 9 41 85.5 29 0.2 29.2 21 0,02 15 0.02 63.4 [10] 10 50 34.2 37 0.84 36.5 ~ 26 [11] 11 26 9.4 11 0.01 57.7 10 § 0,28 § 61.5 [12] 12 37 12.3 22 0. 1 40.5 19 0.08 48.6 [13] 13 42 20.4 16 0.3 61.9 14 0.3 16 0.29 19 § i § 66.7 [13] Mean 47.5 156.6 25.8 1.5 24.6 0,4 23.3 2.0 19.0 15.1 56.5% [13] * Decrease 1 : initial decrease in prostate size during the first 6 months of hormonal treatment.

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

bound PSA. ClinChem 1994; 40:1009. 18. King C, Friese J, Lauren L, Dowell B, Shaw N, Lilja H, et al. Measurement on IMx of free and total forms of prostate-specific antigen for differentiation of patients with benign prostatic hyperplasia and prostate cancer. Clin Chem 1994; 40:1007. 19. Dowell B, King C, Weatherholt J, Schaefer V. Differential recognition of PSA forms is not reflected in the clinical performance of IMx PSA. Presented at XXII Meeting of

PSA. ClinChem 1994; 40:1009. 18. King C, Friese J, Lauren L, Dowell B, Shaw N, Lilja H, et al. Measurement on IMx of free and total forms of prostate-specific antigen for differentiation of patients with benign prostatic hyperplasia and prostate cancer. Clin Chem 1994; 40:1007. 19. Dowell B, King C, Weatherholt J, Schaefer V. Differential recognition of PSA forms is not reflected in the clinical performance of IMx PSA. Presented at XXII Meeting

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5
- **6** Gottschling, Hans-Detlef/et al.: Mu..., 1995, S. 392

ng / ml (median, 9.5 ng / ml), of the 111 patients with benign Prostatahyhyperplasia 7.5 ng / ml (median, 6.3 ng / ml). For this purpose, was a significant difference observed (p <0.0001). Clinically useful to classify the patient population is based on the PSA levels in 3 groups, namely <4 ng / ml, 4-10 ng / ml and> 10 ng / ml (Tab. 10). It was found that the majority (90.5% ) of the preoperative patients with prostate cancer PSA levels> 4 ng / ml showed (Tab. 10 a). In contrast, presented up 33.3% of patients with benign prostatic hyperplasia with a PSA <4 ng / ml. Table 10 A and B: Distribution of 259 patients in PSA groups PSA Group <4 ng / ml: 4-10 ng / ml j > 10 ng / ml j Beng. Prostatahyp. n (%) 37 (33.3) \ 51 (46.0) 23 (20.7) ) 100%

**13%** Einzelplagiatswahrscheinlichkeit



of

mittlere PSA-Wert für Patienten mit GLEASON Grad 4-Anteilen tragenden Karzinomen betrug 14,32 ng/ml (Median 8,55 ng/ml), der der Patienten mit reinem GLEASON Grad 3 Karzinomen 10,38 ng/ml (Median 6,9 ng/ml). Obwohl hier ein Unterschied besteht, ist dieser statistisch nicht signifikant (Tab. 30). i Auch ein signifikanter Unterschied im f-PSA-Anteil zwischen Patienten mit und ohne GLEASON Grad 4-

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strong growth promoters of normal and most cancerous breast tissue; 2) most known risk factors for breast cancer are attributable to some form of estrogen overexposure; [57] 57), 14.1 ng/mL (C-157), 55.1 ng/mL [57] (C-191), and 7.7 ng/mL (C-231). The [57] agreement between the two assays was [57] 10%. [57] It is well-known in the literature that [57] the predominant form of PSA in male [57] serum is PSA

the prostate 24 had peripheral zone hypoechoic defects, all of which were biopsied. Of these patients 3 had cancer. Therefore, cancer was found in 5.5 per cent (3 of 54) of patients with benign prostatic hyperplasia, with a positive biopsy rate of 12.5 per cent (3 of 24). Screening asymptomatic populations is a complex public health issue that encompasses serious unanswered questions regarding the natural history of

einem PSA <4 ng/ml. Tabelle 10 a und b: Aufteilung der 259 Patienten in PSA -Gruppen PSA-Gruppen <4 ng/ml j 4-10 ng/ml I >10 ng/ml beng. Prostatahyp. n (%) : 37 (33,3) | 51 (46,0) | 23 (20,7) j 100% Prostatakarzinorri n (%) ! 14(9,5) [ 74(50,0) | 60 (40,5) I 100% HSA-Gruppen <4 ng/ml 4-10 ng/ml >


- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 63
- **12** Borchert, Gudrun: Elevated Levels o..., 1997, S. #P2#Cthan
- **13** Hodge, K.K./McNeal, J.E./Terris, M...., 1989, S. 0


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Prüfbericht
297751
24.10.2015
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# Textstelle (Prüfdokument) S. 24

Prostate cancer n (%) i 14 (9,5) 74 (50.0) 60 (40.5) | 100% PSA Group <4 ng / ml 4-10 ng / ml > 10 ng / ml Beng. Prostatariyp. n (%) I 3 7 (72.5); 51 (40.8) I 23 (27.7) n (%) 14 (27.5) I 74 (59.2) \ 60 (72.3) 100% 100% 100% 39 4.2.1. 2. Preoperative PSA levels Loading The average PSA level for all 148 patients with established prostate cancer was 26.7 ng / ml (median, 9.5 ng / ml), of the 111 patients with benign Prostatahyhyperplasia 7.5 ng / ml (median, 6.3 ng / ml). For this purpose, was a significant difference observed (p <0.0001). Clinically meaningful to classify the patient population on the basis of PSA levels in 3 groups namely <4 ng / ml, 4-10 ng / ml and> 10 ng / ml (Tab. 10).

**8%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

10 ng/ml beng. Prostatahyp. n (%) 37 (72,5) 51 (40,8) ) 23 (27,7) Prostatakarzinom n (%) 14(27,5) ! 74(59,2) 60 (72,3) 100% 100% Tabelle 10 b zeigt, daß 72,5% aller Patienten mit einem präoperativen PSA-Wert <4 ng/ml eine benigne Prostatahyperplasie und 72,3% mit einem PSA-Wert >10 ng/ml ein Prostatakarzinom

einem PSA <4 [3] ng/ml. [3] Tabelle 10 a und b: Aufteilung der 259 Patienten in PSA-Gruppen [3] PSA-Gruppen [3] <4 ng/ml : [3] 4-10 ng/ml j [3] >10 ng/ml j [3] beng. Prostatahyp. [3] n (%) [3] 37(33,3) \ [3] 51 (46,0) [3] 23(20,7) [3] ) 100% [3] Prostatakarzinom [3] n (%) [3] i 14(9,5) [3] 74 (50,0) [3] 60 (40,5) | [3] 100% [3] PSA-Gruppen [3] <4 ng/ml [3] 4-10 ng/ml [3] >10 ng/ml [3] beng. Prostatariyp. [3] n(%) I [3] 37( 72,5) ; [3] 51 (40,8) I [3] 23 (27,7) [3] Prostatakarzinom [3] n (%) [3] 14(27,5) I [3] 74 (59,2) \ [3] 60 (72,3) [3] 100% [3] 100% [3] 100% [12] 12 i bis 3,5 hg/ml ; [12] 50-59 j. (nj [12] 13 ; bis 4,5 ng/ml ; [12] 60-69 j. (nj [12] 17 j bis 6,5 ng/ml [12] m-m j. (nj [12] ] 16 [10] 10 ng/ml und >10 ng/ml aufgeteilt und nachfolgend nach ihrem Anteil an

mittlere PSA-Wert für Patienten mit GLEASON Grad 4-Anteilen tragenden Karzinomen betrug 14,32 ng/ml (Median 8,55 ng/ml), der der Patienten mit reinem GLEASON Grad 3 Karzinomen 10,38 ng/ml (Median 6,9 ng/ml). Obwohl hier ein Unterschied besteht, ist dieser statistisch nicht signifikant (Tab. 30). i Auch ein signifikanter Unterschied im f-PSA-Anteil zwischen Patienten mit und ohne GLEASON Grad 4-

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strong growth promoters of normal and most cancerous breast tissue; 2) most known risk factors for breast cancer are attributable to some form of estrogen overexposure; [57] 57), 14.1 ng/mL (C-157), 55.1 ng/mL [57] (C-191), and 7.7 ng/mL (C-231). The [57] agreement between the two assays was [57] 10%. [57] It is well-known in the literature that [57] the predominant form of PSA in male [57] serum is

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 39
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. #P#Tumordifferenzierung.#A#
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 63
- **12** Borchert, Gudrun: Elevated Levels o..., 1997, S. #P2#Cthan

# Textstelle (Prüfdokument) S. 25

It was found that the majority (90.5%) of the preoperative patients with prostate cancer PSA levels> 4 ng / ml showed (Tab. 10 a). In contrast, presented up 33.3% of patients with benign prostatic hyperplasia with a PSA <4 ng / ml. Table 10 A and B: Distribution of 259 patients in PSA groups PSA Group <4 ng / ml j 4-10 ng / ml I> 10 ng / ml Beng. Prostatahyp. n (%) : 37 ( 33.3) | 51 (46.0) | 23 (20.7) j 100% Prostatakarzinorri n (%) ! 14 (9.5) [74 (50.0) | 60 (40.5) I 100% HSA Group <4 ng / ml 4-10 ng / ml > 10 ng / ml Beng. Prostatahyp. n (%) 37 (72.5) 51 (40.8)) 23 (27.7) n (%) 14 (27.5) ! 74 (59.2) 60 (72,3) 100% 100% 100% 40 Table 10 B shows that 72.5% of patients with a preoperative PSA level <4 ng / ml, a benign prostatic hyperplasia and 72.3% with a PSA level> 10 ng / ml prostate cancer showed. In the diagnostic 'gray zone' between the PSA rule 4 and 10 ng / ml,

**8%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

PSA

the prostate 24 had peripheral zone hypoechoic defects, all of which were biopsied. Of these patients 3 had cancer. Therefore, cancer was found in 5.5 per cent (3 of 54) of patients with benign prostatic hyperplasia, with a positive biopsy rate of 12.5 per cent (3 of 24). Screening asymptomatic populations is a complex public health issue that encompasses serious unanswered questions regarding the natural history of

Gegensatz dazu präsentierten sich 33,3% der Patienten mit einer benignen Prostatahyperplasie mit einem PSA <4 ng/ml. Tabelle 10 a und b: Aufteilung der 259 Patienten in PSA-Gruppen PSA-Gruppen <4 ng/ml j 4-10 ng/ml I >10 ng/ml beng. Prostatahyp. n (%) : 37 (33,3) | 51 (46,0) | 23 (20,7) j 100% Prostatakarzinorri n (%) ! 14(9,5) [ 74(50,0) | 60 (40,5) I 100% HSA-Gruppen <4 ng/ml 4-10 ng/ml >10 ng/ml beng. Prostatahyp. n (%) 37 (72,5) 51 (40,8) ) 23 (27,7) Prostatakarzinom n (%) 14(27,5) ! 74(59,2) 60 (72,3) 100% 100% Tabelle 10 b zeigt, daß 72,5% aller Patienten mit einem präoperativen PSA-Wert <4 ng/ml eine benigne Prostatahyperplasie und 72,3% mit einem PSA-Wert >10 ng/ml ein Prostatakarzinom

- **13** Hodge, K.K./McNeal, J.E./Terris, M...., 1989, S. 0
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 39

# Textstelle (Prüfdokument) S. 27

levels to the entire collective (n = 236) | Up to 2.5 ng / ml; to 49 j. (nj according to the slide diagnosis benign prostatic hyperplasia or prostate, then the following Distribution (Tab. 13). Table 13: Age Corrected PSA levels, broken down by diagnosis to 2.5 ng / ml to 3.5 ng / ml to 4.5 ng / mL to 6.5 ng j / mi Older (years) 'PCa BPH BPH | PCa | BPH PCa to 49 n (%) (91.6) (8, 4) 50-59 n (%) 9 (69.2) 4 (30.8) I; 60-69 n (%) 70-79 n (%) 10 i 7 i (58.8) | ( 41.2) (43.8) 1 9 (56.2) BPH = benign prostatic hyperplasia; PCa = prostate cancer This is clearly demonstrated an increase in prostate cancer incidence with increasing Age and increasing preoperative PSA level. 42 4.2.1.3. Percentage of free PSA The percentage of free PSA (f-

**7%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

hepatitis ( 65) (136) tumors ( 14) des-7-carboxy prothrombm(AU/ml) 5.0 10.0 50.0 0.3 0.5 1.0 5- 0.1 mplnri gst P:A .t*;ir *' 3 r k ** I :: ..... I 0.. ~ . ~~ ..... ' .... . I 0 . iilii i ..... 1 ..... ~ .... , ( ) : No. of cases can be divided into the following five groups: (1) less than 20 ng/ml, (2) 20 to 400 ng/ml, (3) 400 to 1,000 ng/ml, (4) 1,000 to 10,000 ng/ml, and ( 5 ) greater than 10,000 ng/ml, respectively. Recently, the frequency of AFP-negative or low-level AFP HCC patients has been increasing gradually, and for the

sich folgende Verteilung (Tab. 13). Tabelle 13: Alterskorrigierte PSA-Werte, nach Diagnose aufgeschlüsselt bis 2,5 ng/ml bis 3,5 ng/ml bis 4,5 ng/ml j bis 6, 5 ng/mi Älter (Jahre) ' PCa BPH BPH | PCa | BPH PCa bis 49 n (%) (91,6) (8, 4) 50-59 n(%) 9 (69,2) 4 (30,8) I; 60-69 n(%) 70-79 n(%) 10 i 7 i (58,8) | ( 41,2) (43,8) 1 9 (56,2) BPH=benigne Prostatahyperplasie; PCa= Prostatakarzinom Deutlich zeigt sich eine Zunahme der Prostatakarzinomhäufigkeit mit steigendem Alter und steigendem präoperativen PSA-Wert. 4.2.1.3. Prozentualer Anteil des freien

- **14** Plasma abnormal prothrombin (des-g-..., 1988, S. 1623
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 41

# Textstelle (Prüfdokument) S. 28

PSA fraction> 30%, one of these patients was even a share of more than 50%. Clinically recyclable could therefore not "cut-off" value defined for the percentage of free PSA, above whose prostate cancer was no longer diagnosed. 43 Box Plot Split By: BPH, prostate cancer [ -] BPH PCa Figure 8: Percentage of free PSA (f-PSA%) for patients with benign Prostatic hyperplasia (BPH) or prostate cancer (PCa). Boxplot with median, 10-, 25-, 75- and 9 0-percentiles strength and outliers . 44 The majority of patients presented in the clinical interest PSA area from 4-10 ng / ml, so that a division into 3 groups PSA seemed to

**2%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

PSA und f-PSA% und der Höhe des Testosteron-Wertes (Tab.21). Abbildung 12: Regression-Plot von Testosteron- und LH-Serum Spiegel für Patienten einem Prostatakarzinom. y=1,922+0,852*x; r=0,33, p=0,002. a> =L c 0 W +-< o +-> tu tu H Box Plot Split By: BPH,PCa o BPH PCa Abbildung 13: Serum Testosteron-Spiegel (u.g/1) für Patienten mit benigner Prostatahyperplasie oder Prostatakarzinom. Box-Plot mit Median, 10-, 25-, 75- und 90-iger Perzentilen sowie Ausreißer, Tabelle 21: Korrelationen

for patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 55
- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5

grouped so results for the PSA range 4-10 ng / ml, that 73.6% of patients with an f-PSA% <10% had prostate cancer; on the other hand had 66.7% of Patients with an f-PSA%> 20% a benign prostatic hyperplasia (Tab. 15a) . Table 15a: f-PSA (%) in patients with benign prostatic hyperplasia or prostatakarzinom in the PSA range 4-10 ng / ml f-PSA% <10%; 10-20% > 20% BPH 26.4% 44.7% I 66 . 7% PCa 73.6%; 55.3% 33.3% BPH = benign prostatic hyperplasia; PCa = prostate cancer PSA in the range of> 10 ng / ml 85.5% of all patients with a f-PSA had% <10% a Prostate cancer. In f-PSA% range> 20% there were only 4 patients, so that here an interpretation does not



patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

Prostatakarzinom hatten; andererseits hatten 66,7% der [10] Patienten mit einem f-PSA% >20% eine benigne Prostatahyperplasie (Tab. 15a). [10] Tabelle 15 a: f-PSA (%) bei Patienten mit benigner Prostatahyperplasie oder Prostatakarzinom im PSA-Bereich 4-10 ng/ml [10] f-PSA% [10] <10% ; 10-20% [10] >20% [10] BPH [10] 26,4% I 44,7% [10] 66,7% [10] PCa [10] 73,6% ; 55,3% [10] 33,3% [10] BPH=benigne Prostatahyperplasie; PCa=Prostatakarzinom [10] Im PSA Bereich >10 ng/ml hatten 85,5% aller Patienten mit einem f-PSA% <10% ein [10] Prostatakarzinom. Im f-PSA% Bereich >20% befanden sich nur 4 Patienten, so

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. #P#Tumordifferenzierung.#A#

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Prüfdokument) S. 29

PSA in the range of> 10 ng / ml 85.5% of all patients with a f-PSA had% <10% a Prostate cancer. In f-PSA% range> 20% there were only 4 patients, so that here an interpretation does not seem sensible (Tab. 15 b). Table 15 b: f-PSA (%) in patients with benign prostatic hyperplasia, or prostatakarzinom in the PSA range> 10 ng / ml ' f-PSA% <10%! 10-20%; > 20% BPH 14.5%! 54.2% ; 50% 45 In Table 15 c, in the patients with PSA levels <4 ng / ml are listed sees one that 63.6% of patients with a f-PSA% <10% of prostate cancer and 77. 8% with an f-

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5

## Textstelle (Prüfdokument) S. 29

PSA% <10%! 10-20%; > 20% BPH 14.5%! 54.2%; 50% 45 In Table 15 c, in the patients with PSA levels <4 ng / ml are listed sees one that 63.6% of patients with a f-PSA% <10% of prostate cancer and 77.8% with an f-PSA%> 20% had a benign prostatic hyperplasia. Table 15 c: f-PSA (%) in patients with benign prostatic hyperplasia, or prostatakarzinom in the PSA range <4 ng / ml f-PSA% I <10% I 10-20%) > 20% BPH 36 . 4% 81.8% j 77.8% PCa I 63.6% I 18,2% | 22 .2% To view the value of the f-PSA share one with regard to the differentiation between to assess nem prostate cancer or benign prostatic hyperplasia, achieved - Followed by the determination of the sensitivity and specificity. As

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

mit einem f-PSA% <10% ein Prostatakarzinom und 77,8% mit einem f-PSA% > 20% eine benigne Prostatahyperplasie hatten. Tabelle 15 c: f-PSA (%) bei Patienten mit benigner Prostatahyperplasie oder Prostatakarzinom im PSA-Bereich <4 ng/ml f-PSA% I <10% I 10-20% ) >20% BPH 36,4% 81,8% j 77,8% PCa I 63,6% I 18,2% | 22,2% Um die Wertigkeit des f-PSA-Anteiles hinsichtlich der Differenzierung zwischen einem Prostatakarzinom oder einer benignen Prostatahyperplasie zu beurteilen, er- - folgte die Bestimmung der Sensitivität und

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 45

## Textstelle (Prüfdokument) S. 30

to assess nem prostate cancer or benign prostatic hyperplasia, achieved - Followed by the determination of the sensitivity and specificity. As we have seen, is the Sensitivity 90% and specificity 33% for PSA serum levels> 4.0 ng / ml. Which Analysis of receiver operating characteristic (ROC) curves Alier patient shows that the curve for F-PSA% in clinically significant PSA range a higher sensitivity and specificity (Fig. 9). Only those patients with a PSA level selected 4-10 ng / ml, so show the ROC curves that f-PSA% back

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

is possible." "Why do you want to investigate, then?" SUGGESTED READING [ 1] SWETS J.A., Measuring the accuracy of diagnostic systems. SCIENCE, 240 (1988) 1285-1293. [2] MCNEIL B.J., HANLEY J.A., Statistical approaches to the analysis of receiver operating characteristic (ROC) curves. MED DECIS MAKING, 4 (1984) 137.150. [3] METZ C.E., ROC Methodology in radiologic imaging. INVESTIGATIVE RADIOLOGY, 21 (1986) 720-733. [4] QUINN M.F., Relation of observer agreement to accuracy according to a two-receiver signal detection model

- **15** Ganatra, R./Nofal, M. (Hrsg.): Hand..., 1989, S. 180

## Textstelle (Prüfdokument) S. 30

clearly the sensitivity and specificity superior to PSA (Fig. 10). Furthermore, Sensitivity and specificity were selective for 3 f-PSA% thresholds, namely <10% , <15% and <20%, analyzed (Tab. 16). 46 [1] specificity Figure 9: Receiver operating characteristic (ROC) curves for PSA and fPSA% for all patients with benign prostatic hyperplasia or Prostate cancer (n = 258). 47 lifted, so 90% of patients with prostate cancer, but only 28% recognized with benign prostatic hyperplasia. Eliminating all patients who normwertig according to the agecorrected PSA levels (Table 12 and Tab.13) (they will be counted as described by

1 specificity

**6%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Remarkable among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an

- **12** Borchert, Gudrun: Elevated Levels o..., 1997, S. #P1#Elevated

# Textstelle (Prüfdokument) S. 31

of these patients in 3 groups (<30 cm3, 30-50 cm3 and> 50 cm3 BPH share) shows that no significant Kanter difference in the percentage f-PSA present proportion (p = 0.61) (Fig. 11a, Tab. 18). Table 18: Influence of BPH volume on the f-PSA percentage of patients with a benign prostatic hyperplasia or prostate cancer and a PSA between 's 4-10 ng / ml (n = 118) ------ <30 cm3 I 30-50 cm3 > 5 0 cm3 Mean f-PSA% 13.4% i 14.3% ! i 15% A trend exists only within the PSA area> 10 ng / ml. Prostate glands with a high BPH share (> 50 cm3) ate here on average a higher f-PSA% smaller than Glands, but this also is not significant (p = 0.0928) (Fig.llb,

**6%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

Remarkable among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an

aber, daß auch hier kein signifikanter Unterschied vorliegt (p=0,14). Tabelle 20: Einfluß des BPH-Volumens auf den f-PSA-Anteil für Patienten mit einem Prostatakarzinom im PSA-Bereich 4-10 ng/ml (n=69) < 30 cm3 | 30-50 cm3 j > 50 cm3 Mittelwert f-PSA% 10,7% ; 13,8% I 11,8% Auch für Patienten mit einer benignen Prostatahyperplasie im PSA-Bereich 4-10 ng/ml ergab sich kein signifikanter Unterschied des f-PSA% in den 3 BPH-Gruppen (P-0,51). 4.2.1.5.

- **12** Borchert, Gudrun: Elevated Levels o..., 1997, S. #P1#Elevated
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 52

ng / ml. Prostate glands with a high BPH share (> 50 cm3) ate here on average a higher f-PSA% smaller than Glands, but this also is not significant (p = 0. 0928) (Fig.llb, Table19) 50 CO Q. o <30 0 30-50 o > 50 Figure 11a: Percentage of free PSA (f-PSA%) for patients with benign Prostatic hyperplasia or prostate cancer in the PSA range of 4 to 10 ng / ml, split into 3 BPH groups (<30, 30-50,> 50 com). Box plot with median and 10-, 25-, 75- and 9 0-percentiles strength and outliers. 51 Box plot Split By: Sono BPH classes Inclusion criteria: PSA tot. > 10 ng / ml 0 <30 \ east \ 30-50 13> 50 Figure 11b: Percentage of free PSA (f-PSA%) for patients with benign Prostatic hyperplasia or prostate cancer in the PSA range> 10 ng / ml, split into 3 BPH groups (<30, 30-50,> 50 cc). Box plot with median and 10-, 25-, 75- and 90-percentiles strength and breakaway .; 52 Table 19: Influence of BPH volume on the f-PSA percentage of patients with a benign prostatic hyperplasia or prostate cancer with PSA levels> 10

**21%** Einzelplagiatswahrscheinlichkeit



Remarkable among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an

PSA exceeded that level. At 10 years, distant failure remained at 18% for men with PSA levels of 4.0 ng/ml or less but increased to approximately 40% for the PSA range of 4.1 to 20.0 ng/ml. Only 22% of patients with an initial PSA level greater than 20.0 ng/ ml were distant disease free at 10 years posttreatment. Multivariate analysis of stage, grade, and

benigner Prostatahyperplasie oder Prostatakarzinom im PSA-Bereich 4 bis 10 ng/ml, aufgesplittet in 3 BPH-Gruppen (<30, 30-50, >50 com). Box-Plot mit Median und 10-, 25-, 75- und 90-iger Perzentilen sowie Ausreißer. Box Plot Split By: Sono BPH-Klassen Inclusion criteria: PSA ges. >10 ng/ml 0 <30 \ö\ 30-50 13 >50 Abbildung 11b: Prozentualer Anteil des freien PSA (f-PSA%) für Patienten mit benigner Prostatahyperplasie oder Prostatakarzinom im PSA-Bereich >10ng/

Remarkable among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an

Remarkable among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an


- **12** Borchert, Gudrun: Elevated Levels o..., 1997, S. #P1#Elevated
- **16** Kuban, Deborah A./u.a.: Potential b..., 1995, S. 1
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 51
- **12** Borchert, Gudrun: Elevated Levels o..., 1997, S. #P1#Elevated

## Textstelle (Prüfdokument) S. 32

ng / ml (n = 65) 30 cm3 30-50 cm3 > 50 cm3 Mean f-PSA% 8 . 7% I I 9.1% I 14.1% ! Theoretically interesting the influence of ultrasound certain BPH Proportion of the prostate to the f-PSA proportion in patients with It would be conceivable namely an increase of f-PSA share with growth of benign

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

aber, daß auch hier kein signifikanter Unterschied vorliegt (p=0,14). Tabelle 20: Einfluß des BPH-Volumens auf den f-PSA-Anteil für Patienten mit einem Prostatakarzinom im PSA-Bereich 4-10 ng/ml (n=69) < 30 cm3 | 30-50 cm3 j > 50 cm3 Mittelwert f-PSA% 10,7% ; 13,8% I 11,8% Auch für Patienten mit einer benignen Prostatahyperplasie im PSA-Bereich 4-10 ng/ml ergab sich kein signifikanter Unterschied des f-PSA% in den 3 BPH-Gruppen (P-0,51). 4.2.1.5.

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 52

# Textstelle (Prüfdokument) S. 33

benign gen BPH share. Table 20 shows, however, that even here there was no significant under- Arbitration is present (p = 0.14) . Table 20: Influence of BPH volume on the f-PSA percentage of patients with a Prostate cancer in PSA range 4-10 ng / ml (n = 69) <30 cm3 | 30-50 cm3 j> 5 0 cm3 Mean f-PSA% 10.7%; 13.8% I 11.8% Even for patients with benign prostatic hyperplasia in PSA range 4-10 ng / ml, there was no significant difference of f-PSA% in the 3 BPH groups (P-0.51). 53 4.2.1.5. Hormonal influence of testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) to the PSA and f-PSA in prostate cancer and benign Prostatic hyperplasia Of 148 of 259 patients (57%) were serum testosterone, LH and FSH levels before. Of these, 53 patients had benign prostatic hyperplasia and 95 patients prostate cancer. First, the dependence of the testosterone level was of the gonadotropic Pituitary hormones

**13%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

aber, daß auch hier kein signifikanter Unterschied vorliegt (p=0,14). Tabelle 20: Einfluß des BPH-Volumens auf den f-PSA-Anteil für Patienten mit einem Prostatakarzinom im PSA-Bereich 4-10 ng/ml (n=69) < 30 cm3 | 30-50 cm3 j > 50 cm3 Mittelwert f-PSA% 10,7% ; 13,8% I 11,8% Auch für Patienten mit einer benignen Prostatahyperplasie im PSA-Bereich 4-10 ng/ml ergab sich kein signifikanter Unterschied des f-PSA% in den 3 BPH-Gruppen (P-0,51). 4.2.1.5.

for patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

as a diet-restricted control (Chapin et al., 1982). Animals with ad lib access to feed and water were used as an untreated control group. Plasma levels of testosterone, luteinizing hormone (LH), and follicle stimulating hormone (FSH) were measured by radioimmunoassay using a commercial preparation ( testosterone) or kits generously provided by the N.I.A.M.D.D. and Dr. A. F. Parlow (LH and FSH). For histologic evaluation, animals were

superoxide dismutase (MnSOD) genotype, and lung cancer risk. J Occup Environ Med, 46, 556-64. Wang MC, Guo MF, Zhao GQ (2006). Research on mRNA expression level of MnSOD gene in prostate cancer and benign prostatic hyperplasia tissue. Chin J Gerontol, 26, 164-5. Wang S, Wang F, Shi X, et al (2009). Association between manganese superoxide dismutase (MnSOD) Val-9Ala polymorphism and cancer risk-A meta-analysis. Eur J Cancer, 45, 2874-81. Wang Y,

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 52
- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5
- **17** 2. Lymphokine Assays A. MIF B. IFN ..., 1982, S. 377
- **18** Sun, Guo-Gui/u.a.: Different Associ..., 1937, S. #P7#cigarette

## Textstelle (Prüfdokument) S. 33

The majority of LH and testosterone levels move but within the wide reference ranges (Fig. 12). In contrast Set this was a similar correlation for patients with benign Are not found prostatic hyperplasia (p = 0.54 and p = 0.22). For the 53 patients with benign prostatic hyperplasia and 95 patients with prostate cancer was no significant difference (p = 0.36) of Testo be determined steron values < <(Fig. 13). Furthermore, it is for both groups of patients no dependence between the height PSA and the PSA-f% and the amount of testosterone

**5%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Papers Technical Options in Complex Ureteral Lesions: 273 'Ureter-Sparing' Surgery Passerini-Glazel, G.; Meneghini, A.; Aragona, F.; Oliva, G.; Milani, C; Pagano, F. Serum Prostate-Specific Antigen Discriminates Weakly 281 between Men with Benign Prostatic Hyperplasia and Patients with Organ-Confined Prostate Cancer Sershon, P.D.; Barry, M.J.; Oesterling, J.E. Prostate-Specific Antigen Density: A Means to Enhance Detec- 288 tion of Prostate Cancer Ramon, J.; Boccon-Gibod, L.; Billebaud, T.; Astier, L.; Kobelinsky, M.;

- **19** class gs ctg2 von uni-muenchen.deun..., 1994, S. 4

# Textstelle (Prüfdokument) S. 34

Furthermore, it is for both groups of patients no dependence between the height PSA and the PSA-f% and the amount of testosterone value (Tab.21). 54 Figure 12: Regression plot of testosterone and LH serum levels for patients y = [1] .922 + 0.852 * x; r = 0.33, p = 0.002. 55 a> = L c 0 W + - < o + -> tu tu H Box Plot Split By: BPH, prostate cancer 0 BPH _l Al] PCa Figure 13: Serum testosterone levels (ug / 1) for patients with benign Prostatic hyperplasia or prostate cancer. Boxplot with median, 10-, 25-, 75- and 90-percentiles strength and outliers, 56 Table 21: Correlations between testosterone and PSA and f-PSA% in patients th with benign prostatic hyperplasia (n = 53) or prostate cancer (n = 95) Correlation p-value benign Prostatahyperpiasie pTostÄntWterzlhom 1 testosterone - PSA 0,31 j testosterone - f-PSAE% 0.55 4.2.1.6. Hormonal influence of dihydrotestosterone (DHT) on the PSA and f-PSA in prostate cancer and benign Prostatic hyperplasia the ~ T14 separate patients were in addition to the testosterone, LH and FSH the dihydrotestosterone serum levels determined. Of these, 58 had (50.8%) papatients with prostate cancer and 56 (49.2%) a benign prostatic hyperplasia. 23 (39.6%) of 58 patients with prostate cancer underwent radical

1 testosterone - PSA

**10%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

Höhe des PSA und f-PSA% und der Höhe des Testosteron-Wertes (Tab.21). Abbildung 12: Regression-Plot von Testosteron- und LH-Serum Spiegel für Patienten einem Prostatakarzinom. y=1,922+0,852*x; r=0,33, p=0,002. a> =L c 0 W +-< o +-> tu tu H Box Plot Split By: BPH,PCa o BPH PCa Abbildung 13: Serum Testosteron-Spiegel (u.g/1) für Patienten mit benigner Prostatahyperplasie oder Prostatakarzinom. Box-Plot mit Median, 10-, 25-, 75- und 90-iger Perzentilen sowie Ausreißer, Tabelle 21: Korrelationen

Remarkable among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an

among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an

superoxide dismutase (MnSOD) genotype, and lung cancer risk. J Occup Environ Med, 46, 556-64. Wang MC, Guo MF, Zhao GQ (2006). Research on mRNA expression level of MnSOD gene in prostate cancer and benign prostatic hyperplasia tissue. Chin J Gerontol, 26, 164-5. Wang S, Wang F, Shi X, et al (2009). Association between manganese superoxide dismutase (MnSOD) Val-9Ala polymorphism and cancer risk-A meta-analysis. Eur J Cancer, 45, 2874-81. Wang Y,

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 55
- **12** Borchert, Gudrun: Elevated Levels o..., 1997, S. #P1#Elevated
- **18** Sun, Guo-Gui/u.a.: Different Associ..., 1937, S. #P7#cigarette

# Textstelle (Prüfdokument) S. 35

shown in Table 22nd 57 Table 22: Testosterone (Testo), dihydrotestosterone ( DHT), luteinizing hormone mon (LH) and follicle-stimulating hormone (FSH) for patients with benign prostatahyperplasie (n = 56) or prostate cancer (n = 58) Serum parameters Benign Prostate (Mean) Prostate | Carcinoma Hyperplasia p-value Testo (u.g / 1) 4.5 3.5 0.32 DHT (pg / ml) 469 . 2 434.1 0.39 LH (IU / 1) 7.0 I 7.1 0.92 FSH (IU / 1) 11. 6 10.9 0 . 76 For the diagnostic groups (benign prostatic hyperplasia vs. prostate cancer) were the no significant differences in the level of average testosterone, DHT, LH and FSH serum levels observed (Tab. 22). There was a correlation (p ~ <0.0001) zwischerTder amount of testosterone and dihydrotestosterone in the serum in patients with benign prostatic hyperplasia (Fig.14), whereas this not the case for patients with prostate cancer (p = 0.68) . The level of PSA serum levels did not correlate with the amount of dihydrotestosterone steron serum levels neither in patients with benign prostatic hyperplasia (p = 0.28) nor in those with prostate cancer (p = 0.77). Subdivided to the Patients, so did their diagnosis within groups in different PSA Group also no significant differences with respect to the level of serum DHT levels, find (Tab. 23) . 58 CD Q. I- I Q 1400 - 1200 1000 i 3 4 5 6 7 8 Testosterone (u.g / 1) Figure 14: Regression plot of testosterone and dihydrotestosterone (DHT) for Patients with benign prostatic hyperplasia, y = 1,474 + 103.9 * x; r = 0.73, p <0.0001. 59 Table 23: DHT averages for different groups of patients with PSA benign prostatic hyperplasia or prostate cancer PSA Group

**4%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

Testo), Dihydrotestosteron (DHT), Luteinisierendes Hormon (LH) und Follikelstimulierendes Hormon (FSH) für Patienten mit benigner Prostatahyperplasie (n=56) oder Prostatakarzinom (n=58) Serumparameter benigne Prostata- (Mittelwert) Prostata- | karzinom hyperplasie p-Wert Testo ( u.g/1) 4,5 3,5 0,32 DHT (pg/ml) 469,2 434,1 0,39 LH (IU/1) 7,0 I 7,1 0,92 FSH ( IU/1) 11,6 10,9 0,76 Für die Diagnosegruppen (benigne Prostatahyperplasie vs. Prostatakarzinom) wurden keine signifikanten Unterschiede in der Höhe der mittleren Testosteron-, DHT-, LH- und FSH-Serumspiegel festgestellt (Tab. 22) . Es

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

for patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ,

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 57
- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5

## Textstelle (Prüfdokument) S. 36

DHT (pg / ml) DHT (pg / ml) (ng / ml) Benign prostate Prostate Hyperplasia carcinoma p-value <4 507 552 0 . 74 4-10 476 404 0.61 > 10 429 440 0.65 The same studies have been described for the percentage, free PSA fraction expects, with no correlation to the percentage of DHT Serumsplegels Proportion of free PSA for patients with benign prostatic hyperplasia (p = 0.11) as also demonstrated with a prostate cancer (p = 0.51). Comparing the Level of DHT serum levels of different percentage thresholds of the free PSA Anteifes so fin A ~ ebehfalls errMh iri ~ both DiAngnosegruppen no Si gnifikanzen (Tab. 24). Table 24: DHT

● **4%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

und Dihydrotestosteron (DHT) für Patienten mit einer benignen Prostatahyperplasie. y=1,474+103,9*x; r=0,73, p<0,0001. Tabelle 23: DHT-Mittelwerte für unterschiedliche PSA-Gruppen bei Patienten mit benigner Prostatahyperplasie oder Prostatakarzinom PSA-Gruppen DHT (pg/ml) DHT ( pg/ml) (ng/ml) benigne Prostata- Prostatahyperplasie karzinom p-Wert <4 507 552 0,74 4 bis 10 476 404 0,61 >10 429 440 0,65 Die gleichen Untersuchungen wurden für den prozentualen, freien PSA-Anteil berechnet, wobei sich keine Korrelation des DHT-Serumsplegels zum

for patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 59
- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5

# Textstelle (Prüfdokument) S. 37

Comparing the Level of DHT serum levels of different percentage thresholds of the free PSA Anteifes so fin A ~ ebehfalls errMh iri ~ both DiAngnosegruppen no Si gnifikanzen (Tab. 24). Table 24: DHT averages for different f-PSA thresholds in patients with benign prostatic hyperplasia or prostate cancer f-PSA DHT (pg / ml) DHT (pg / ml) Threshold Benign prostate Prostate Hyperplasia carcinoma p-value <10% 364 475 0.13 10-20% 498 379 0,20 > 20% 514 466 0 . 43 4.2.2. Prostate cancer staging 4.2.2.1. Age distribution Of the 148 patients in whom prostate biopsies a systematic prostatakarzinom was diagnosed, 74 patients were in clinically localized Carcinoma with histologically negative lymph nodes of

● **5%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

Remarkable among these four patients was the observation that their serum PSA level was in the same range as the serum PSA level of male patients with benign prostatic hyperplasia or prostate cancer. The age of the four patients was 31 years (patient C-57), 42 years (C-157), 39 years (C-191), and 28 years (C-231). Patients C-157, C-191, and C-231 had two to four children, and patient C-57 had had an

so finden sich ebenfalls in den beiden Diägnosegruppen keinerlei Signifikanzen (Tab. 24). Tabelle 24: DHT-Mittelwerte für unterschiedliche f-PSA Schwellen bei Patienten mit benigner Prostatahyperplasie oder Prostatakarzinom f-PSA DHT (pg/ml) DHT (pg/ml) Schwelle benigne Prostata- Prostatahyperplasie karzinom p-Wert <10% 364 475 0,13 10-20% 498 379 0, 20 >20% 514 466 0,43 4.2.2. Prostatakarzinom-Staging 4.2.2.1. Altersverteilung Von den 148 Patienten, bei denen durch systematische Prostatabiopsien ein Prostatakarzinom diagnostiziert wurde, wurden 74 Patienten bei klinisch

- **12** Borchert, Gudrun: Elevated Levels o..., 1997, S. #P1#Elevated
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 59

# Textstelle (Prüfdokument) S. 38

in both pathological stages pT2 and pT3. No patient underwent surgery in stage pT4. 61 Table 26: Pathologic stages in 74 prostatectomy Stage pT2 pT3 n 1 38 36 % 51. 4 48.6 4.2.2.3. Influence of pathological stages to the preoperative PSA The median PSA was for patients with prostate cancer who are not radical Prostatectomies "were (mean 41.6 ng / ml; Median 11.2 ng / ml) significantly higher (p <0.0004) than that of those who were radically prostatectomy (means 11.8 ng / ml; metal dian 7.4 ng / ml). The division of all radical prostatectomy patients after their preoperative PSA values a <a <showed in the 3 clinical interest PSA

**2%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

hormonal treatment. Decrease 2: maximal decrease in prostate size achieved during treatment. [13] t Prostate size in grams. [13] PSA in ng/mL. [13] § Progression of disease (by PSA). [13] and 66 patients with prostate cancer who repeatedly underwent TRUS volume measurements of [13] the prostate. The men were treated either with surgical castration or radiation therapy; however, the [13] latter study included the

mittlere PSA-Wert für Patienten mit GLEASON Grad 4-Anteilen tragenden Karzinomen betrug 14,32 ng/ml (Median 8,55 ng/ml), der der Patienten mit reinem GLEASON Grad 3 Karzinomen 10,38 ng/ml (Median 6,9 ng/ml). Obwohl hier ein Unterschied besteht, ist dieser statistisch nicht signifikant (Tab. 30). i Auch ein signifikanter Unterschied im f-PSA-Anteil zwischen Patienten mit und ohne GLEASON Grad 4-

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 63

# Textstelle (Prüfdokument) S. 39

Group that 73% of all patients had PSA values a <a <up to 10 ng / ml. Almost 15% of patients presented oriented with normwertigem PSA before surgery ( Tab.27). Table 27: Preoperative PSA levels in 74 radical prostatectomy patients divided into 3 groups PSA <4 ng / ml 4-10 ng / ml > 10 ng / ml n 11 43 20 % 14.9 58.1 27 62 Analyzes pathological tumor stages in terms of rising PSA levels one, it can be seen that patients with pT3-stage significantly higher preoperative PSA levels had as patients with pT2 stages (p = 0.0038). Table 28 shows the Distribution of pathological stages in the 3 PSA Group. Table 28: Pathologic stages and divided into 3 PSA groups (n = 74) <4 ng / ml 4-10 ng / ml > 10 ng / ml pT2; n 7 26 5 (%) 18. 4% 68. 4% 13.2% pT3; n 4 17 15 (%) 11.1% 47.2% 41. 7% It was also found that patients with higher pathologic tumor stages a signifi- cantly larger tumor volume showed (p <0.0001) 4.2.2. 4. Influence of pathological stages on the f-PSA Clinically interesting is the question of whether with increasing pathologic stage

**3%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

hatten als Patienten mit pT2-Stadien (p=0,0038). Tabelle 28 zeigt die Verteilung der pathologischen Stadien in die 3 PSA-Gruppen. Tabelle 28: Pathologische Stadien und Aufteilung in 3 PSA-Gruppen (n=74) <4 ng/ml 4-10 ng/ml >10 ng/ml pT2; n 7 26 5 (%) 18,4% 68,4% 13,2% pT3; n 4 17 15 (%) 11,1% 47,2% 41,7% Es zeigte sich auch, daß Patienten mit pathologisch höheren Tumorstadien ein signifikant größeres Tumorvolumen aufwiesen (p<0, 0001), 4.2.2.4. Einfluß der pathologischen Stadien auf das f-PSA Klinisch

hatten als Patienten mit pT2-Stadien (p=0,0038). Tabelle 28 zeigt die Verteilung der pathologischen Stadien in die 3 PSA-Gruppen. Tabelle 28: Pathologische Stadien und Aufteilung in 3 PSA-Gruppen (n=74) <4 ng/ml 4-10 ng/ml >10 ng/ml pT2; n 7 26 5 (%) 18,4% 68,4% 13,2% pT3; n 4 17 15 (%) 11,1% 47,2% 41,7% Es zeigte sich auch, daß Patienten mit pathologisch höheren Tumorstadien ein signifikant größeres Tumorvolumen aufwiesen (p<0, 0001), 4.2.2.4. Einfluß der pathologischen Stadien auf das f-PSA Klinisch interessant ist

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 62

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## Textstelle (Prüfdokument) S. 40

GLEASON system (s. [3] .2.2.), Which also Gleason grade 4 percentage of the tumor was determined. 24 of 74 patients (32.4%) reported ever to Gleason grade 4 Shares in carcinoma. The mean PSA level supporting for patients with Gleason grade 4 Shares carcinomas was 14.32 ng / ml (median 8.55 ng / ml), of the patient with pure Gleason grade (ng / ml) f-PSA (%) with Gleason grade 4 14.3 11. 9 without Gleason grade 4 10.38 11. 0 p-value 0 .07 0.60 4.2.2.6. Hormonal influence of testosterone on pathological stages and Grading Continues to explore the behavior of the testosterone level was within the Group of patients with prostate cancer who were radical prostatectomy den.-There was ~ fAHnJa A A lAl Anlis7e7fA!T AA no significant Difference in the level of testosterone levels between the pathological StadipT2 and pT3 en (p = 0.33) ( Fig. 15). Similar to the above investigation carried out on the pathological stages results furthermore no link between the tumors with and without GLEASON Grade 4 Shares and

3 carcinogens

**3%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

mittlere PSA-Wert für Patienten mit GLEASON Grad 4-Anteilen tragenden Karzinomen betrug 14,32 ng/ml (Median 8,55 ng/ml), der der Patienten mit reinem GLEASON Grad 3 Karzinomen 10,38 ng/ml (Median 6,9 ng/ml). Obwohl hier ein Unterschied besteht, ist dieser statistisch nicht signifikant (Tab. 30). i Auch ein signifikanter Unterschied im f-PSA-Anteil zwischen Patienten mit und ohne GLEASON Grad 4-

In squamous cell carcinomas the 5 year cumulative-survival rate of patients with moderate PLK expression was 45.7% whereas that of the group with high PLK expression was 24.1% (P=0.01). Within the group of patients with squamous cell carcinomas we observed an equal distribution of post surgical stages comparing patients with moderate and high PLK expression. In adenocarcinomas, the Kaplan-Meier

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 63
- **20** Prognostic significance of polo-lik..., 1997, S. 546

# Textstelle (Prüfdokument) S. 41

with and without GLEASON Grade 4 Shares and the testosterone levels (p = 0. 70). The mean testosterone for tumors with Gleason grade 4 Shares is only slightly to the Gleason grade 3 tumors increased (Fig. 16). 65 Figure 15: Testosterone serum levels (ug / l) in patients with prostate cancer after radical prostatectomy. Split in histological stages pT2 and pT3. Boxplot with median, 10-, 25-, 75- and 90-percentiles strength and outliers. 66 CD c o 1w o 00 CD H- Box Plot Grouping Variable: Gleason grade Inclusion criteria: PCa-OP Gleason score <7 Gleason score> 7 Figure 16: Testosterone serum levels (ug / 1) for patients with prostate cancer after radical prostatectomy. Split into cancers with Gleason score <7 and>. 7 Boxplot with median, 10-, 25-, 75- and 9 0-percentiles strength and outliers. 67 4.2.2.7. Hormonal influence of dihydrotestosterone to pathological Stadiums and Grading Among the 114 patients, for which there was a dihydrotestosteronevalue, was at par-

**6%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

proportional to the volume of intracapsular as well as extracapsular prostate cancer in the untreated patient. 1" PSA has proven to be particularly useful in following patients with prostate cancer after radical prostatectomy,8 10 after radiotherapy to the prostate, " and after anti-androgen therapy.12 Like p30, prostate specific antigen is unique to the prostate gland and semen. It has an

GLEASON Grad 3-Tumoren erhöht (Abb. 16). Abbildung 15: Testosteron Serum-Spiegel (ug/l) für Patienten mit einem Prostatakarzinom nach radikaler Prostatektomie. Aufgesplittet in histologische Stadien pT2 und pT3. CD c o 1 w o 00 CD h- Box Plot Grouping Variable: GLEASON-Grad Inclusion criteria: PCa-OP GLEASON-Summe <7 GLEASON-Summe >7 Abbildung 16: Testosteron Serum-Spiegel (u.g/1) für Patienten mit einem Prostatakarzinom nach radikaler Prostatektomie. Aufgesplittet in Karzinome mit GLEASON-Summe <7 und >7. 4.2.2.7. Hormoneller Einfluß von

proportional to the volume of intracapsular as well as extracapsular prostate cancer in the untreated patient. 1" PSA has proven to be particularly useful in following patients with prostate cancer after radical prostatectomy,8 10 after radiotherapy to the prostate, " and after anti-androgen therapy.12 Like p30, prostate specific antigen is unique to the prostate gland and semen. It has an

- **21** Graves, H.C.B., Kamarei, M., Stamey..., 1990, S. 0
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 66
- **21** Graves, H.C.B., Kamarei, M., Stamey..., 1990, S. 0

# Textstelle (Prüfdokument) S. 43

which there was a dihydrotestosteronevalue, was at par- Overall, [58] patients ( 50.2%) were diagnosed with prostate cancer. Again, 23 of possibly the sensitivity and specificity of PSA increase further. The experiments presented here were during a re- Research stay at Stanford University, Department of Urology, Stanford, California, U.S.A. performed. It could for the first time the prostate specific antigene in free, unbound form from the serum of patients with prostatic be norrrrsoliert and characterized. Previously wÄardieses succeeded only ejaculate (Schaller et al., 1987). Prostate specific antigen which is determined by an immune assay, consists of the sum of the free, unbound, and the a-1antichymotrypsin of bound

58 patients (39.6%) had a localized prostate cancer and underwent

**4%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

einer benignen Prostatahyperplasie vorliegen und möglicherweise die Sensitivität und Spezifität des PSA weiter erhöhen. Die hier vorgelegten experimentellen Untersuchungen wurden während eines Forschungsaufenthaltes an der Stanford University, Department of Urology, Stanford, California, U.S.A. durchgeführt. Es konnte erstmalig das Prostata-spezifische Antigen in freier, ungebundener Form aus Serum von Patienten mit einem Prostatakarzinorrrrsoliert und charakterisiert werden. Bisher wärdieses nur

acid phosphatase found in the prostate is unique for that organ in those species. We found it possible to precipitate acid phosphatase of prostatic origin from the serum of patients with prostatic carcinoma9 and we also found that metastatic prostatic carcinoma to lymph nodes would be detected by gel diffusion studies (Figure 10-1). Moncure et al. have applied

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 68
- **22** Tannenbaum, Mayron: Urologie Pathol..., 1977, S. 204

## Textstelle (Prüfdokument) S. 43

immune assay, consists of the sum of the free, unbound, and the a-1antichymotrypsin of bound form. Since it is known that the free fraction of PSA in patients with prostate cancer only about 5 to 15% is (LILJA et al., 1991; Stamey et al., 1994; STENMAN et al., 1991), it was necessary, sera with very high overall PSA values ä <ä <to use. This is usually in patients with metastatic th, untreated or refractory prostate cancer before. Through several gelchromatographic processes were 230 ml serum with a PSA

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

ungebundenen und der an a-1-Antichymotrypsin gebundenen Form. Da bekannt ist, daß die freie Fraktion des PSA bei Patienten mit einem Prostatakarzinom nur ca. 5 bis 15% beträgt (LILJA et al., 1991; STAMEY et al., 1994; STENMAN et al., 1991), war es notwendig, Sera mit sehr hohen Gesamt-PSA-Werten zu verwenden. Dieses liegt in der Regel bei Patienten mit metastasierten, unbehandelten oder therapierefraktären Prostatakarzinomen

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 68

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## Textstelle (Prüfdokument) S. 43

with very high overall PSA values ä <ä <to use. This is usually in patients with metastatic th, untreated or refractory prostate cancer before. Through several gelchromatographic processes were 230 ml serum with a PSA concentration> 2000 ng / ml in patients with metastatic prostate cancer 69 separated. After isolation of the free PSA and its share concentration as the final product was 0. 5 ml of free PSA at a concentration of 27,000 ng / ml obtained, which corresponded to 5.6% of the initial PSA total concentration.

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Flutamide + bilateral orchiectomy 9 29 [71] .5 Flutamide + leuprolide 4 13 Total 31 1 O0 procedures and radiation or hormonal therapy. In 1989, Stamey et al. 6 reported a mean net-PSA decrease of 95% in previously untreated patients with metastatic prostate cancer disease undergoing hormonal therapy. It is also well known that the prostate size decreases during androgen suppression, 2,3,7 a finding usually confirmed by digital rectal examination. However,

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 31

## Textstelle (Prüfdokument) S. 45

Macroglobulin (MG) (LILJA, 1985; Lundwall and LILJA, 1987). The molecular weights of these complexes are much higher than that of the PSA and between 90 and 100 kDa for the PSA-ACT complex and around 780 kDa for PSA-MGcomplex (Chen et al, 1995a;. LILJA et al., 1991). By means of an immunoassay, however, can only be detected at ACT complexed form. Complex compounds to MG probably can not therefore be recognized by an immune assay, as the tetrameric structure of the MG

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Komplexe sind wesentlich höher als das des PSA und liegen zwischen 90 und 100 kDa für den PSA-ACT-Komplex und um 780 kDa für PSA-MG-Komplex ( CHEN et al., 1995a; LILJA et al., 1991). Mittels eines Immun-Assays kann jedoch nur die an ACT komplexierte Form nachgewiesen werden. Komplexverbindungen zu MG können vermutlich deshalb nicht von einem Immun-Assay

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 71

## Textstelle (Prüfdokument) S. 45

is known that "clipping" of the PSA between tween the remnants 145/146 leads to inactivation, which is also for the positions Is believed 85/86 and 182/183 (Lundwall and LILJA, 1987). That "clipped" protein migrates with an intact PSA during SDS-PAGE (WATT et al., this se eluded the detection of the methods used, or the supply spent primary monoclonal antibodies against PSA (F5) could not zymogen recognize. It thus appears that the zymogen form of biochemical with "routine" 'method in

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

den Resten 145/146 zur Inaktivierung führt, was ebenfalls für die Positionen 85/86 und 182/183 angenommen wird (LUNDWALL und LILJA, 1987). Das " geclippte" Protein wandert mit intaktem PSA während der SDS-PAGE (WATT et al., Die Zymogen-Form konnte im Serum nicht nachgewiesen werden, was die Theorie untermauert, daß PSA aktiviert wird, bevor es in den Blutkreislauf gelangt. Dieses würde

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 71

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## Textstelle (Prüfdokument) S. 46

inhibitor was done, although this is present in abundance in serum are. Incubating the ejaculate from insulated, free PSA in female serum, so it comes to form equimolar PSA complexes in descending concentration: (PSA JMI> ( f-PSA) -> _ (PSA-ACT). (Chen et al-1995b; Christensson efAnl., 1990) . Only about 70% of the isolated PSA from ejaculate are enzymatically active and therefore capable, Forming complexes. MG binds rapidly to active PSA, so that thereof remains available for little complexation to ACT. The relatively

**2%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Überfluß vorhanden sind. Inkubiert man aus Ejakulat isoliertes, freies PSA in weibliches Serum, so kommt es zur Ausbildung äquimolarer PSA-Komplexe in absteigender Konzentration: (PSAjmi >.(f-PSA)-> (PSA-ACT) (CHEN et al. -1995b; CHRISTENSSON efäl., 1990). Nur ca. 70% des isolierten PSA aus Ejakulat sind enzymatisch aktiv und somit fähig, Komplexe auszubilden. MG bindet sich sehr schnell an aktives PSA, so

1 Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 72

## Textstelle (Prüfdokument) S. 46

to the 30% already present inactive PSA ("clipped" Form). Prostate-specific antigen is considered to be the most sensitive serum marker for men with prostataerkrankungen. For clinical use is generally accepted that PSA is formed exclusively by the epithelial cells of the prostate. Since PSA but both in benign (benign prostatic hyperplasia, bacterial prostatitis) and malignancies may be increased, there is no defined PSA serum Mirror, which excludes or confirmed one way or another condition - PSA is therefore

**3%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

model to study gene expression in the human prostate, PA cDNAs and the corresponding gene were isolated. PA was chosen, because it is exclusively synthesized by the epithelial cells of the prostate. In Chapter 11 the isolation of three different PA cDNAs from a PC 82 prostate eDNA library is described. Oligonucleotides deduced from the PA amino acid sequence were

- **3** Riegman, Pieter: Prostate-specific ..., 1992, S. 128

# Textstelle (Prüfdokument) S. 46

Further, a variety of clinical showed 73 Prostate cancer studies that PSA alone little accurate staging information delivery Fert, in particular, since the tumor volume for the individual patient preoperative can not be safely estimated ( Noldus and Stamey, 1996a; PARTIN et al., 1993a; . Stamey et al, 1987; Stamey et al., 1989a). Different molecular forms of serum PSA were recently described (Christensson et al., 1993; ulja, 1993b; STENMAN et al., [1991] ). The investigation tions of these forms have shown that the proportion of the complexed to ACT PSA is lower in patients with benign prostatic hyperplasia than patient ducks, where prostate cancer is present, although here overlaps proof are (Christensson et al., 1993; LILJA, 1993b;. STENMAN et al, In the clinical part of this work the importance of free PSA has been to share Differentiation between benign and malignant prostate disease parmore in the diagnostic "gray zone" of PSA 4-10 ng / ml and the

1991) . So it appears that the specificity of the PSA through

**5%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

Prostatakarzinom-Studien, daß PSA allein wenig akkurate Staginginformationen liefert, insbesondere, da das Tumorvolumen für den individuellen Patienten präoperativ nicht sicher abgeschätzt werden kann ( NOLDUS und STAMEY, 1996a; PARTIN et al., 1993a; STAMEY et al., 1987; STAMEY et al., 1989a). Verschiedene molekulare Formen des Serum-PSA wurden kürzlich beschrieben (CHRISTENSSON et al., 1993; ULJA, 1993b; STENMAN et al., [1991] ). Die Untersuchungen dieser Formen haben ergeben, daß der Anteil des an ACT komplexierten PSA bei Patienten mit einer benignen Prostatahyperplasie niedriger ist als bei Patienten,

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

ACT komplexierten PSA bei Patienten mit einer benignen Prostatahyperplasie niedriger ist als bei Patienten, bei denen ein Prostatakarzinom vorliegt, obwohl auch hier Überlappungen nachzuweisen sind (CHRISTENSSON et al., 1993; LILJA, 1993b; STENMAN et al., Die vorliegenden Untersuchungen haben gezeigt, daß Patienten mit einer benignen Prostatahyperplasie einen signifikant niedrigeren, mittleren PSA-Wert als Patienten mit einem Prostatakarzinom aufwiesen. Bei 72% aller

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 73
- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 73

## Textstelle (Prüfdokument) S. 47

type and size by the result of histological diagnosis Value of determination of the f-PSA in prostate cancer and share the description nignen prostatic hyperplasia can be accurately judged. 74 The present studies have shown that patients with benign Prostatic hyperplasia significantly lower, middle PSA levels than patients had a prostate cancer. In 72% of all patients preoperatively with a tive PSA <4 ng / ml were diagnosed with benign prostatic hyperplasia. 72% of patients with a PSA level> 10 ng / ml showed prostate

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5

# Textstelle (Prüfdokument) S. 47

can be enced. The proportion of free, unbound PSA was in patients with a benign process statahyperplasie significantly higher in patients with prostate cancer. These ses were also other authors show (LILJA et al., 1991; and PRESTIGIACOMO Stamey, 1995; . Stamey et al, 1994; STENMAN et al., 1991). It could continue shown werdenrdaAY no "" cut7AS[ff "Tevet for Ifen f-PSA Anfeil 'exists, therefore above Sen no more prostate cancer was diagnosed. Below the f-PSA threshold of 10% and with increasing total PSA increased the rate of patients with a prostate cancer. For the total PSA range < 4 ng / ml was found in 63.6% of cases a carcinoma, for the PSA range 4-10 ng / ml in 73.6% and more than 10 ng / ml in 85.5% of cases. In contrast, had the above-mentioned PSA ranges 67%, 50% and 78% of patients had a benign prostate disease, when the f-PSAshare was greater than 20%. The analyzes of the ROC curves, particularly in the clinical interesting PSA "gray zone" 4-10 ng / ml, have higher sensitivities th and specificities for the percentage of free PSA compared to PSA demonstrated. It has also been shown that the sensitivity and spespecificity highest for the threshold was <10% f-PSA percentage, which means that 78% were detected of patients with benign prostatic hyperplasia right from Test the. In other words, but this also means that 22% of patients falsely had been diagnosed and possibly treated. If one were sawn 75 Mood of the PSA and f-PSA proportion as the sole

**2%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

bei Patienten mit einer benignen Prostatahyperplasie signifikant höher als bei Patienten mit einem Prostatakarzinom. Dieses konnten auch andere Autoren zeigen (LILJA et al., 1991; PRESTIGIACOMO und STAMEY, 1995; STAMEY et al., 1994; STENMAN et al., 1991). Es konnte weiterhin gezeigt werdenrdaß kein""cut7öff" teveT für Ifen f-PSA-Anfeil 'existiert, oberhalb dessen kein Prostatakarzinom mehr diagnostiziert wurde. Unterhalb der f-PSA-Schwelle

patients with benign prostatic hyperplasia. J Urol 150: 90- 94, 1993. 13. Eri LM, and Tveter KJ: A prospective, placebocontrolled study of the luteinizing hormone-releasing hormone agonist leuprolide as treatment for patients with benign prostatic hyperplasia. J Urol 150: 359-364, 1993. 14. Carpentier PJ, Schroeder FH, and Blohm JHM: Transrectal uhrasonography in the followup of prostatic arcinoma patients. J Urol 128: 742-746, 1982. 15. Carpentier PJ, and Schroeder FH: Transrectal ultrasonography

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 74
- **2** Noldus, Joachim: /Ferrari M. Prestigiacomo A. Stamey..., 1996, S. 5

## Textstelle (Prüfdokument) S. 48

significantly, is the routine determination of f-PSA-share as a complementary study to Determination of total PSA, in particular in the clinically relevant PSA "Gray zone", justified. For clinical practice, this means that in patients independently with PSA values a <a <between 4 and 10 ng / ml and an f-PSA fraction <10% the outcome of rectal examination of the prostate (DRE) Prostate Biopsies should be carried out. Patients with an unremarkable DRE, a PSA Serum levels 4-10 ng / ml and an f-PSA fraction> 20% may fall

**3%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

of PSA added 0 20 40 60 80 YANG P-PSA (ng/ml) fig. 2. Comparison of serum PSA values by Yang P-PSA and Hybritech M-PSA intermedial* range of PSA. Patient sera with PSA values between 3 and 80 ng./ml. by the Yang P-PSA te6t were assayed in tandem by both tests, first using respective PSA kit calibrators and then using independent PSA calibrator. Each

- **21** Graves, H.C.B., Kamarei, M., Stamey..., 1990, S. 0

## Textstelle (Prüfdokument) S. 48

patients with a Prostatakarcarcinoma, a higher proportion complex bound PSA as in patients with a particular nignen prostatic hyperplasia is present. BJARTELL and co-workers studied therefore semi immunohistochemistry the a-1-antichymotrypsin content in the stroma, in neuroenclAlkTinen TBasalzellen cells and epithelial cells of the prostate gland (BJARTELL et al., 1993). They were able to prove, that a large part of the PSA prostate carcinoma cells and ACT produced, whereas virtually no ACT of PSA-producing Could be detected in epithelial cells of

● **3%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

of epicardial afferent terminals 51 b. Effect of kinins on coronary vasculature and circulation 51 C. Cardioprotective actions of kinins 52 2. Functional importance in myocardial ischaemia and infarction 52 F. Spermatozoa, Sertoli cells, and epithelial cells of the prostate, epididymis, and coagulating glands 52 1. Kininogenases 52 a. Tissue kallikrein-like proteases 52 i. Cellular localisation 53 2. Kininases 53 3. Kininogens and kinins 53 G. Leucocytes 53 1. Kininogenases 53 a. Leucokininogenases 54 b. Neutral kininogenases 54 2. Identification of tissue killikrein and

• **23** Bioregulation of kinins: kallikrein..., 1992, S. 3

## Textstelle (Prüfdokument) S. 49

al. studied in a retrospective study the Influence of the f-PSA proportion to the sensitivity of a screening collective (Catalona et al., 1995). Of these sera were from 63 men with benign Prostate and examined 50 men with prostate cancer ( Catalona et al., 1991; Catalona et al., 1993). Interestingly, this was Working Group a significant difference in the free PSA fraction in patients with prostate cancer with large (> 40cm3) and small (<40cm3) Prostatavolumen. If f-PSA " cut off" of <13.7% 90% of patients had a Prostate cancer have

● **1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

haben jedoch gezeigt, daß nicht 50%, sondern nur 10% aller asymptomatischen Männer in der Altersgruppe ab 50 Jahren einen PSA-Wert von >4,0 ng/ml aufweisen (ANDRIOLE und CATALONA, 1993; CATALONA et al., 1991; CATALONA et al., 1993). Bei diesen Männern mit PSA-Werten in der " Grauzone" (4-10 ng/ml) wurde mittels Biopsie in 22% bis 27% ein Prostatakarzinom gesichert. Lag der PSA-Wert >10 ng/ml,

● **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 3

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## Textstelle (Prüfdokument) S. 50

collected serum samples as opposed to the study of Catalona and employees ( Catalona et al., 1995). One, the influence of androgens on the growth of the prostate and the development nes prostate cancer is well known (CABOT, 1896; Huggins et al. 1941 WHITE, 1893). This testosterone is the predominant, circulating arrival drugs in men. It is among more than 90% of the Leydig cells of the testis Secreted influence of luteinizing hormone. Numerous affect androgens che physiological parameters in the

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Studie von CATALONA und Mitarbeiter (CATALONA et al., 1995). Der Einfluß der Androgene auf das Wachstum der Prostata und die Entwicklung eines Prostatakarzinoms ist hinreichend bekannt (CABOT, 1896; HUGGINS et al., 1941; WHITE, 1893). Dabei ist Testosteron das vorherrschende, zirkulierende Androgen beim Mann. Es wird zu über 90% von den Leydigzellen des Hodens unter Einfluß des Luteinisierenden Hormons sezerniert. Androgene

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 77

# Textstelle (Prüfdokument) S. 51

of 3.5 ng / ml / cm3 calculated (Stamey et al, 1989a.); this ratio was based on a highly significant correlation (r = 0.70) between serum PSA levels and Carcinoma volume. The same ratio was for patients with prostate benign tahyperplasie 10-fold lower (0.3 ng / ml / cm3) (Stamey et al., 1987). Furthermore, many large studies may show in prostate cancer, the PSA that Serum levels with increasing clinical stage, tumor volume and pathological rule stage correlated (Osterling et al, 1988;. PARTIN et al, 1990;. Stamey et al., 1987; Stamey and Kabalin, 1989). Furthermore, is considered certain that the Preoperative-Stagtng A A by introducing such histological Grading of the preoperative prostate biopsies and assessment of the clinical Stage in the rectal examination, can be improved (and KLEER

**3%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

Quotient basierte auf einer hoch signifikanten Korrelation (r=0,70) zwischen Serum-PSA-Spiegel und Karzinomvolumen. Der gleiche Quotient lag für Patienten mit einer benignen Prostatahyperplasie 10-fach niedriger (0,3 ng/ml/ cm3) (STAMEY et al., 1987). Weiterhin haben viele große Studien beim Prostatakarzinom zeigen können, daß der PSA- Serumspiegel mit zunehmendem klinischen Stadium, Tumorvolumen und pathologischen Stadium korreliert ( OESTERLING et al., 1988;

beim Prostatakarzinom Viele große Studien haben für das Prostatakarzinom zeigen können, daß der PSA- Serumspiegel mit zunehmendem klinischen Stadium, pathologischen Stadium und Tumorvolumen korreliert (OESTERLING et al., 1988; PARTIN et al., 1990; STAMEY et al., 1987; STAMEY und KABALIN, 1989). Trotzdem ist PSA allein nicht so spezifisch, daß es für den individuellen Patienten eine akkurate, alleinige Staginginformation liefert ( NOLDUS und STAMEY, 1996). Die Genauigkeit

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 79
- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 7

## Textstelle (Prüfdokument) S. 52

to improve the preoperative staging. 80 Studies on free PSA for the individual staging in prostate cancer do not yet exist in the literature prior to radical prostatectomy. Stamey et al. could on pooled sera from patients with prostate cancer before radical prostate tektomie show that no significant difference in the level of PSA-ACT Commission plex and therefore not free PSA-share between the Prostate loading limited (pT2) and the prostate capsule pierced tumors (pT3) standing (Stamey et al., 1994). Our investigation of non-pooled sera shown that

**3%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

PSA level after removal of the prostate [9] (table 2) and 2) the first voided urine PSA level is much higher [9] than the midstream urine PSA level in patients with prostate [9] cancer before radical prostatectomy and in controls. Tremblay [9] et al also found urinary PSA levels to be the highest in the first [9] 30 cc of voided urine from a 25-year-old

- **24** Iwakiri, J., Granbois, K., Wehner, ..., 1993, S. #P#received

## Textstelle (Prüfdokument) S. 52

the determination of LH, FSH, Testosterone and dihydrotestosterone serum levels without clinical relevance for the Distinguishing between benign prostatic hyperplasia and prostate cancer 81 6. Summary Prostate specific antigen (PSA) is an organ specific marker, both in benign and malignant diseases of the prostate can be increased, PSA is composed of 237 amino acids serine protease with a molecular weight of approximately 28 kDa. PSA is androgen from the epithelium of the prostate glands produced. In prostate cancer, the PSA serum levels

**3%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

Indirect cutane- 172. ous immunofluorescence. I. Morphologic observations in bullous diseases, malignancies and connective tissue diseases. Arch. Dermatol. 105:52, 1972. 173. 155. Ablin, R. J.: Antiepithelial antibodies in the serum of patients with benign and malignant diseases of the prostate. Z. Immunitaetsforsch. 173a 146:8, 1973. 156. Ablin, R. J.: Demonstration of intercellular and basement-membrane zone antibodies in benign prostatic hypertrophy. Dermatol gica 146:163, 1973. 157. Bystryn, J-C, et al.: Antibodies against the 174. cytoplasm of human

- **22** Tannenbaum, Mayron: Urologie Pathol..., 1977, S. 89

# Textstelle (Prüfdokument) S. 53

patients with prostatic nom as well as benign prostatic hyperplasia. The specificity of the PSA is well with low. Almost all biochemical studies on PSA were on from ejaculate w A nen PSA cfuTcn A fAHrTrTTcTa it hreTfnlfiilliAHTenfAnch "higher concentration (0.5 5 mg / ml) than is present in the serum. The amino acid sequence is also made Ejakulat- PSA known. PSA exists in two different forms measurable in serum. On Much of the PSA is bonded to the protease inhibitor a-1antichymotrypsin, the Remainder is in free, unbound form. Bound The difference in proportion ner / unbound PSA percentage can be diagnostically in benign and malignant Exploit diseases of the prostate. In the present study experimentally succeeded for the first time by means of several gelchromatographischer filtrations the isolation of the free, unbound PSA of seconds rum of patients with prostate cancer to the amino acid sequencing. It it could be shown that the free PSA in the serum of patients with a per statakarzinom both in the "mature" form with 237 amino acids, as well as in the "nicked" -form. The latter refers to a group within the molecule probably 82 to inactivate made separation. Inactive preforming the PSA (zymogen), the are suspected on the basis

**0%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

simulation. F I G U R E 3 . T V screen photograph at a moment of a simulated landing approach. may be used for visibil i ty zero-landing in the future. The novel methods described permit for the first time by means of an accessory system to the flight instruments of an aircraft the generation of extremely well focused, high-contrast, color-true stylized images on standard T V screens

other hand data on these determining factors are very difficult to obtain. E.g. as a result of a large study on the safety of stairs (Heimplaetzer et al, 1988) it could be shown that the frequencies of falling from stairs are more associated with the type of household than with the type of stairs. Households with younger children show a uniform

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- **25** 17. Analytic Evaluation of Display ..., 1971, S. 199
- **26** Impact assessment methodologies for..., 1989, S. 102
- **27** Pseudomonas-infected cystic fibrosi..., 1983, S. #P7#bacteriolysis.#A#

## Textstelle (Prüfdokument) S. 53

in the age distribution of the overall total of 259 patients not collective distinguished, still was the influence of the strongest androgen dihydrotestosterone steron (DHT) on serum PSA levels and free PSA fraction in patients examined with benign prostatic hyperplasia and prostate cancer. The sensitivity of PSA in a standard limit <4 ng / ml was 90%, specificity jedoch- nur.bei-33% a patients with benignsignificantly Prostatahyperplasiehatterreinerr higher, mean free PSA fraction than patients with a Prostatakarcarcinoma. In clinical interest PSA range of 4-10 ng / ml 73. 6%

**3%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Originalquellen)

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- **6** Gottschling, Hans-Detlef/et al.: Mu..., 1995, S. 392

# Textstelle (Prüfdokument) S. 4

(Carter et al., 1992; Schmid et al., 1993). The underlying idea is [1993] that the [1993] Growth rate of benign and malignant prostate tissue by [1993] serial measurements of PSA may be estimated, because the PSA level [1993] with [1993] the volume of the epithelial cells of the prostate gland correlates.

1993). The disadvantages of PSAD-determination based on the

1993). The disadvantages of PSAD-determination based on the

1993). The disadvantages of PSAD-determination based on the

1993). The disadvantages of PSAD-determination based on the

1993). The disadvantages of PSAD-determination based on the

**4%** Einzelplagiatswahrscheinlichkeit

# Textstelle (Originalquellen)

unterschiedlichen, möglicherweise auch altersbedingt veränderten Volumen-Relation von Prostataepithel zu Prostatastroma. 3. PSA-Velocity / PSA Verdopplungszeit: Diese Parameter beurteilen den PSA-Verlauf über einen bestimmten Zeitraum (CARTER et al., 1992; SCHMID et al., 1993). Die zugrunde liegende Idee ist, daß die Wachstumsgeschwindigkeit von benignem und malignem Prostatagewebe durch serielle Messungen des PSA-Wertes abgeschätzt werden kann, da der PSA-

al., 1988). Both the PA and hGK-1 gene are completely sequenced, their mutual homology is 82% (Schedlich et al., 1987; Riegman et al., 1989). PA is exclusively synthesized by the epithelial cells of the prostate gland (Wang et al. , 1979,1981; Watt et al., 1986; Gallee et al., 1986). Its presumed function is dissolving the seminal coagulum by digesting proteins secreted by the seminal vesicles,

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 6
- **3** Riegman, Pieter: Prostate-specific ..., 1992, S. 66

## Textstelle (Prüfdokument) S. 40

men 10.38 ng / ml (median, 6.9 ng / ml). Although there is a

## Textstelle (Originalquellen)

mittlere PSA-Wert für Patienten mit GLEASON Grad 4-Anteilen tragenden Karzinomen betrug 14,32 ng/ml (Median 8,55 ng/ml), der der Patienten mit reinem GLEASON Grad 3 Karzinomen 10,38 ng/ml (Median 6,9 ng/ml). Obwohl hier ein Unterschied besteht, ist dieser statistisch nicht signifikant (Tab. 30). i Auch ein signifikanter Unterschied im f-PSA-Anteil zwischen Patienten mit und ohne GLEASON Grad 4-

- **1** Noldus, Joachim: Experimentelle und klinische Unters..., 1996, S. 63

**1%** Einzelplagiatswahrscheinlichkeit

## Textstelle (Prüfdokument) S. 42

are present in patients with benign prostatic hyperplasia and

## Textstelle (Originalquellen)

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- **5** Oesterling, J.E./Cooner, W.H., Jaco..., 1993, S. 679

**3%** Einzelplagiatswahrscheinlichkeit

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Worte: 730 (von 14.079) = 6 %

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# Glossar



| | |
|---|---|
| • Ampel | Entsprechend der Gesamtwahrscheinlichkeit wird ein Rating der Schwere durch die Ampelfarbe berechnet: grün (bis 19 %) = wenige Indizien unterhalb der Bagatellschwelle; gelb (20 bis 49 %) - deutliche Indizien enthalten, die eine Plagiatsbegutachtung durch den Prüfer notwendig machen; rot (ab 50 %) = Plagiate liegen mit sehr hoher Wahrscheinlichkeit vor, die eine Täuschungsabsicht dokumentieren. Bei publizierten Dissertationen sollte ein offizielles Verfahren zur Prüfung und/oder zum Entzug des Doktortitels eröffnet werden. |
| • Anteil Fremdtexte (brutto) | Anteil aller durch die Software automatisch gefundenen Bestandteile aus anderen Texten am Prüftext (von mindestens 7 Wörtern) in Prozent und Anzahl der Wörter gemessen. Dabei wird noch keine Interpretation auf Plagiatsindizien oder korrekte Übernahmen (z.B. Zitat, Literaturquelle) vorgenommen. |
| • Anzahl Fremdtext (netto) | Anteil aller durch die Software automatisch gefundenen und als Plagiatsindizien interpretierten Bestandteile aus anderen Texten am Prüftext (von mindestens 7 Wörtern) in Prozent und Anzahl der Wörter gemessen. |
| • Bauernopfer | Fehlende Quellenangabe bei einer inhaltlichen oder wörtlichen Textübernahme, wobei die Originalquelle an anderer Stelle des Textes (außerhalb des Absatzes, des Satzes, des Hablsatzes oder des Wortes) angegeben wird. |
| • Compilation | Zusammensetzen des Textes als "Patchwork" aus verschiedenen nicht oder unzureichend zitierten Quellen. |
| • Eigenplagiat | Übernahme eines eigenen Textes des Autors ohne oder mit unzureichender Kennzeichnung des Autors. Auch wenn hier nur eigene Texte und Gedanken übernommen werden, handelt es sich um eine Täuschung. Der Prüfer geht davon aus, dass es sich hier um neue Texte und Gedanken des Autors handelt. |
| • Einzelplagiatswahrscheinlichkeit | Grobe Berechnung der Wahrscheinlichkeit des Vorliegens eines Plagiates des einzelnen Treffers (oder der Treffer) auf einer Seite im Prüfbericht. |
| • Gesamtplagiatswahrscheinlich-keit | Berechnung der Wahrscheinlichkeit des Vorliegens von Plagiaten durch Verknüpfung der Indizienanzahl, des Netto-Fremdtextanteils und der Schwere der |

# Glossar

einzelnen Plagiatsindizien.

- **Ghostwritersuche** — Über den statistischen Vergleich der Texte (Stilometrie) wird eine Wahrscheinlichkeit berechnet, ob die Texte von demselben Autor stammen.
- **Indizien** — Dieser Prüfbericht gibt nur die von der Software automatisch ermittelten Indizien auf eine bestimmte Plagiatsart wieder. Die Feststellung eines Plagiats kann nur durch den Gutachter erfolgen.
- **Literaturanalyse** — Die im Prüftext enthaltenen Literatureinträge im Literaturverzeichnis werden analysiert: Wird die Quelle im Text zitiert? Handelt es sich um eine wissenschaftliche Quelle? Wie alt sind die Quellen?
- **Mischplagiat - eine Quelle** — Der Text wird hierbei aus verschiedenen Versatzstücken einer einzigen Quelle zusammengesetzt, also gemischt.
- **Mischplagiat - mehrere Quellen** — Der Text wird hierbei aus verschiedenen Versatzstücken aus verschiedenen Quellen zusammengesetzt, also gemischt.
- **Phrase** — Die übernommenen Textstellen stellen allgemeintypische oder fachspezifische Wortkombinationen der deutschen Sprache dar, die viele Autoren üblicherweise verwenden. Solche Übernahmen gelten nicht als Plagiate.
- **Plagiat** — Übernahme von Leistungen wie Ideen, Daten oder Texten von anderen - ohne vollständige oder ausreichende Angabe der Originalquelle.
- **Plagiatsanalyse** — Gefundene gleiche Textstellen (= Treffer) werden durch die Software automatisch auf spezifische Plagiatsindizien analysiert.
- **Plagiatssuche** — Mit Hilfe von Suchmaschinen wird im Internet, in der Nationalbibliothek und im eigenen Dokumentenbestand nach Originalquellen mit gleichen oder ähnlichen Textstellen gesucht. Diese Quellen werden alle vollständig Wort für Wort mit dem Prüftext verglichen. Plagiatsindizien werden für Textstellen ab 7 Wörtern berechnet.

# Glossar



- **Plagiatswahrscheinlichkeit** — Grobe Berechnung der Wahrscheinlichkeit des Vorliegens eines Plagiates auf der Basis der Plagiatsindizien. Die Ampel zeigt drei Ergebnisse an: grün - keine Wahrscheinlichkeit des Vorliegens eines Plagiates und somit keine weitere Überprüfung notwendig, gelb - mögliches Vorliegen eines Plagiates und somit eine weitere Überprüfung empfohlen, rot - hohe Wahrscheinlichkeit des Vorliegens eines Plagiates und somit weitere Überprüfung unbedingt notwendig.
- **Stilometrie** — Texte werden dabei einzeln nach statistischen Kennzahlen (z.B. durchschnitliche Länge der Wörter, Häufigkeit bestimmter Wörter) analysiert. Sind diese Kennzahlen für zwei Texte ähnlich, liegt hier statistisch der gleiche "Stil" und somit mit hoher Sicherheit der selbe Autor vor.
- **Teilplagiat** — Ein Textbestandteil einer Quelle wurde vollständig ohne ausreichende Zitierung kopiert.
- **Textanalyse** — Der einzelne Text wird durch die Software automatisch für sich allein analysiert, z.B nach statistischen Kennzahlen, benutzter Literatur, Rechtschreibfehlern oder Bestandteilen. Je nach Stand der Softwareentwicklung sind die absoluten Ergebnisse (z.B. Erkennung von Abbildungen, Fußnoten, Tabellen, Zitaten) im einzelnen eingeschränkt aussagefähig. Aufgrund der immer für alle Texte durchgeführten Analysen sind die relativen Unterschiede zwischen den Spalten (z.B. Diplomarbeit vs. Dissertation) uneingeschränkt aussagefähig.
- **Textvergleich** — Jeder Text wird mit anderen älteren Texten vollständig verglichen. Gefundene gleiche Texstellen werden in einem weiteren Schritt z.B. auf Plagiatsindizien hin untersucht.
- **Übersetzungsplagiat** — Nutzung eines fremdsprachigen Textes durch Übersetzung.
- **Verschleierung** — Ein Text wird ohne eindeutige Kennzeichnung (i.d.R. durch Anführungszeichen) Wort für Wort übernommen, aber mit Angabe der Quelle in der Fußnote. Dadurch wird der Prüfer getäuscht, der von einer nur inhaltlichen Übernahme ausgehen muss.
- **Vollplagiat** — Der gesamte Text wird vollständig ohne Zitierung kopiert.

# Glossar



| | |
|---|---|
| • Zitat - wörtlich | Übernommener Text wird z.B. mit Anführungszeichen korrekt dargestellt. Dieses wörtliche Zitat darf keine Veränderungen, Ergänzungen oder Auslassungen enthalten. Fehlt für das Zitat nach der Plagiatssuche ein Nachweis in einer Originalquelle, so wird der Treffer als "Zitat-wörtlich-im Text" bezeichnet. |
| • Zitat - wörtlich - Veränderung | Einzelne Wörter einer korrekt gekennzeichneten wörtlichen Übernahme werden verändert oder weggelassen, ohne dass der Sinn verändert wird. Z.B.: " Unternehmung" wird durch "Unternehmen" ersetzt. |
| • Zitat - wörtlich - Verdrehung | In dem korrekt gekennzeichneten übernommenen wörtlichen Text wird der Sinn durch Austauschung einzelner Wörter deutlich verändert. Beispiel: " überentwickelten" statt "unterentwickelten". |
| • Zitierungsfehler | Arbeitsbezeichnung für eine wörtliche Textübernahme, die nur als inhaltliche Textübernahme (Paraphrase) gekennzeichnet wird. |