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Functional outcomes after treatment for Prostate Cancer

SASRO 5.7.2013

Michael Mark, OA Onkologie/Hämatologie,
Kantonsspital GR

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Overview

- Disease background
- Surgery
- Radiotherapy
- Endocrine Therapy

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Epidemiology CH 2008

Die häufigsten Krebsarten (Inzidenz)

Männer		Frauen	
Prostatakrebs	30 % [§]	Brustkrebs	32.3 %
Lungenkrebs	13 %	Dickdarmkrebs	11.3 %
Dickdarmkrebs	11.5 %	Lungenkrebs	7.4 %
Blasenkrebs	4.6 %	Gebärmutterkörperkrebs	5.8 %
Malignes Melanom (Schwarzer Hautkrebs)	4.6 %	Malignes Melanom (Schwarzer Hautkrebs)	5.5 %

[§] Lesebeispiel: 30 % aller Krebserkrankungen bei Männern betreffen die Prostata

Die Krebsarten mit der grössten Sterblichkeit (Mortalität)

Männer		Frauen	
Lungenkrebs	23.3 % [#]	Brustkrebs	19.6 %
Prostatakrebs	15.2 %	Lungenkrebs	12 %
Dickdarmkrebs	9.8 %	Dickdarmkrebs	10.9 %
Krebs der Bauchspeicheldrüse (Pankreaskarzinom)	5.3 %	Krebs der Bauchspeicheldrüse (Pankreaskarzinom)	7 %
Leberkrebs	4.4 %	Eierstockkrebs (Ovarialkarzinom)	6.2 %

[#] Lesebeispiel: 23.3 % aller Männer, die infolge von Krebs sterben, sterben an Lungenkrebs

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Stage-Classification Prostate-Cancer (PCa)

- TNM Classification: T1a – 2c N0
  - versus locally advanced PCa (T3/4, high risk und N +)
  - metastatic PCa
- Risk groups

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Risk groups: localized PCa

	PSA		Gleason		Stage
Low Risk	<10	*and*	≤ 6	*and*	T1-T2a (T1-2)
Intermediate Risk	10-20	*or*	7	*or*	T2b-T2c (T1-2 + G7)
High Risk	>20	*or*	8-10	*or*	T3-T4

D'Amico et al JCO 1999, ; Graham et al BMJ 2008

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Therapy localized PCa

- Radical prostatectomy
- Radiotherapy
- Active Surveillance
- Watchful waiting

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Therapy metastatic PCa

- Endocrine therapy
- Palliative chemotherapy
- Antiresorptive therapy (bone metastasis)
- Symptomatic treatments (Radiotherapy, Analgesia)

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Surgery

- Radical prostatecomy
- Da-Vinci-Prostatectomy
- "nerve sparing„ surgery

Abbildung 1:
Die Da-Vinci-Technologie besteht aus einer Arbeitskonsole (links) und dem Roboterstativ (rechts). Das Stativ hält die Kamera und zwei bis drei Instrumentenarme. Der Chirurg führt die Instrumente von der Konsole mit dreidimensionaler Sicht und voller Bewegungsfreiheit.

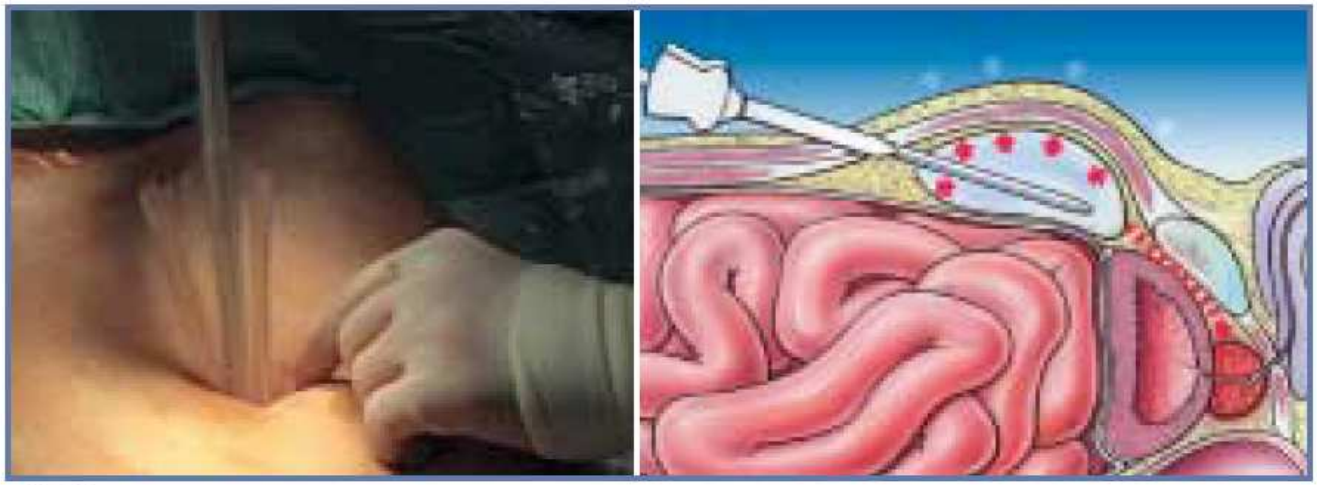

Abbildung 2:
Vorteile des extraperitonealen Zugangs: weniger Kopftieflage, Verhinderung von potenziellen intraperitonealen Komplikationen und peritonealen Reizungen.

Schweizer Zeitschrift für Onkologie 1/2008

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Radiotherapy

- Percutaneous Radiotherapy
  - –With (neo-)adjuvant endocrine therapy
  - –3-D-conformal radiation therapy
  - –IMRT (Intensity Modulated Radiotherapy)
- Brachytherapy
  - – Low dose rate brachytherapy
  - – High dose rate brachytherapy (afterloading)

"Targeted therapy"

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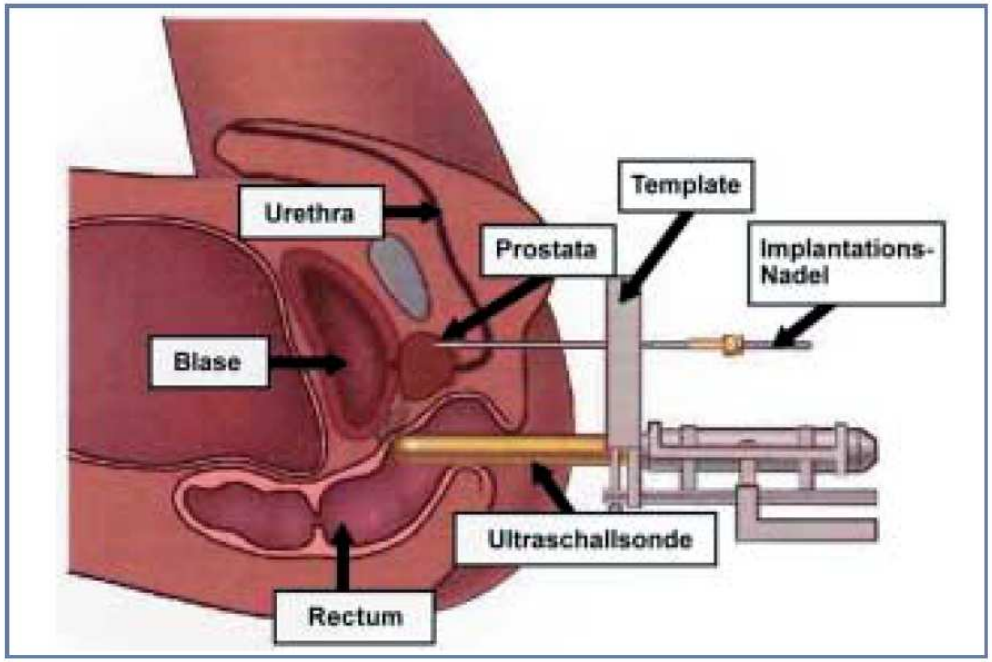

Abbildung 2: Schematische Darstellung der transperinealen Implantation von Hohlnadeln (Applikatoren) bei der Brachytherapie

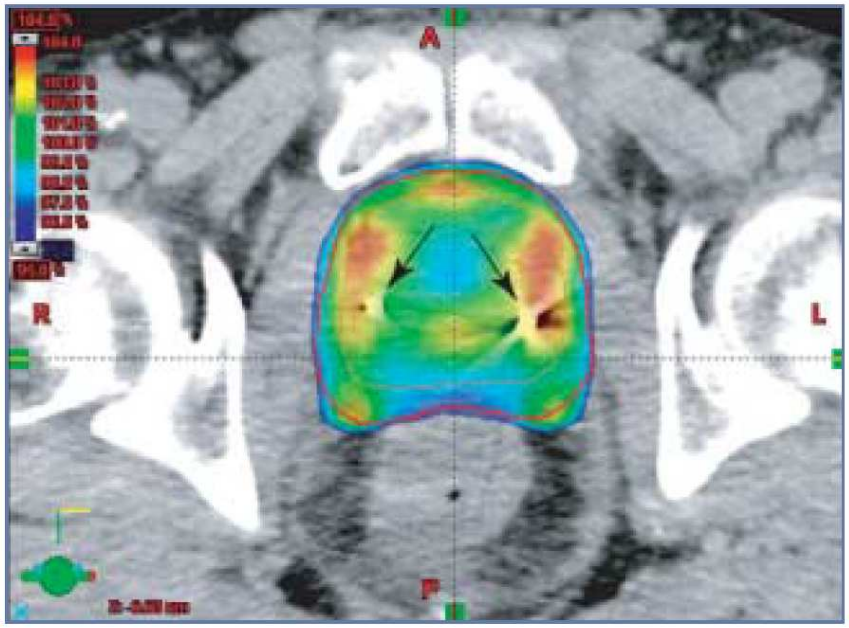

Abbildung 1: Verbesserte Konformität der Dosisverteilung durch intensitätsmodulierte Radiotherapie: Gute Übereinstimmung des Verlaufs des 95%-Dosis-Levels (blaue Einfärbung) mit dem Zielvolumen (rote Linie); die beiden Pfeile markieren implantierte Goldmarker zur Positionskontrolle.

Schweizer Zeitschrift für Onkologie 1/2008

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Long term functional outcomes surgery/radiotherapy

Table 2. Survey Responses on Selected Items Regarding Urinary, Bowel, and Sexual Function.*

Outcome	Prostatectomy	Radiotherapy	Adjusted Odds Ratio (95% CI)†
	percent		
Urinary incontinence			
No control or frequent urinary leakage			
2 yr	9.6	3.2	6.22 (1.92–20.29)
5 yr	13.4	4.4	5.10 (2.29–11.36)
15 yr	18.3	9.4	2.34 (0.88–6.23)
Bothered by dripping or leaking urine‡			
2 yr	10.6	2.4	5.86 (1.93–17.64)
5 yr	12.9	2.9	7.66 (2.97–19.89)
15 yr	17.1	18.4	0.87 (0.41–1.80)
Sexual function			
Erection insufficient for intercourse			
2 yr	78.8	60.8	3.46 (1.93–6.17)
5 yr	75.7	71.9	1.96 (1.05–3.63)
15 yr	87.0	93.9	0.38 (0.12–1.22)
Bothered by sexual dysfunction‡			
2 yr	55.5	48.2	1.19 (0.77–1.86)
5 yr	46.7	39.7	1.48 (0.92–2.39)
15 yr	43.5	37.7	1.33 (0.58–3.03)
Bowel function			
Bowel urgency			
2 yr	13.6	34.0	0.39 (0.22–0.68)
5 yr	16.3	31.3	0.47 (0.26–0.84)
15 yr	21.9	35.8	0.98 (0.45–2.14)
Bothered by frequent bowel movements, pain, or urgency‡			
2 yr	2.9	7.9	0.37 (0.14–0.96)
5 yr	4.4	5.8	0.93 (0.27–3.22)
15 yr	5.2	16.0	0.29 (0.11–0.78)

NEJM 2013;368:436-45.

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Endocrine therapy (ADT)

- Bilaterale orchiectomy
- LHRH-Agonists
- Anti-Androgenes
  - 5α-Reductase-Inhibitors
- Oestrogenes
- Different combinations
- continous - intermittent

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Side effects ADT 1

- Patient's view:
  - „Big Three“:
    - Libido ⬇
    - Erectile dysfunktion (impotence)
    - Hot flushes
  - What you feel:
    - Fatigue, loss of energy, depression, cognitive impairments
  - What you see:
    - Weight gain (fat), loss of muscles, gynecomastia, hair changes, downsizing of penis and testicles

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Side effects ADT 2

- Doctor's view:
  - What you don't see:
    - Osteoporosis
    - Metabolic syndrome
    - Anemia
    - QT-Prolongation (Anti-Androgenes)

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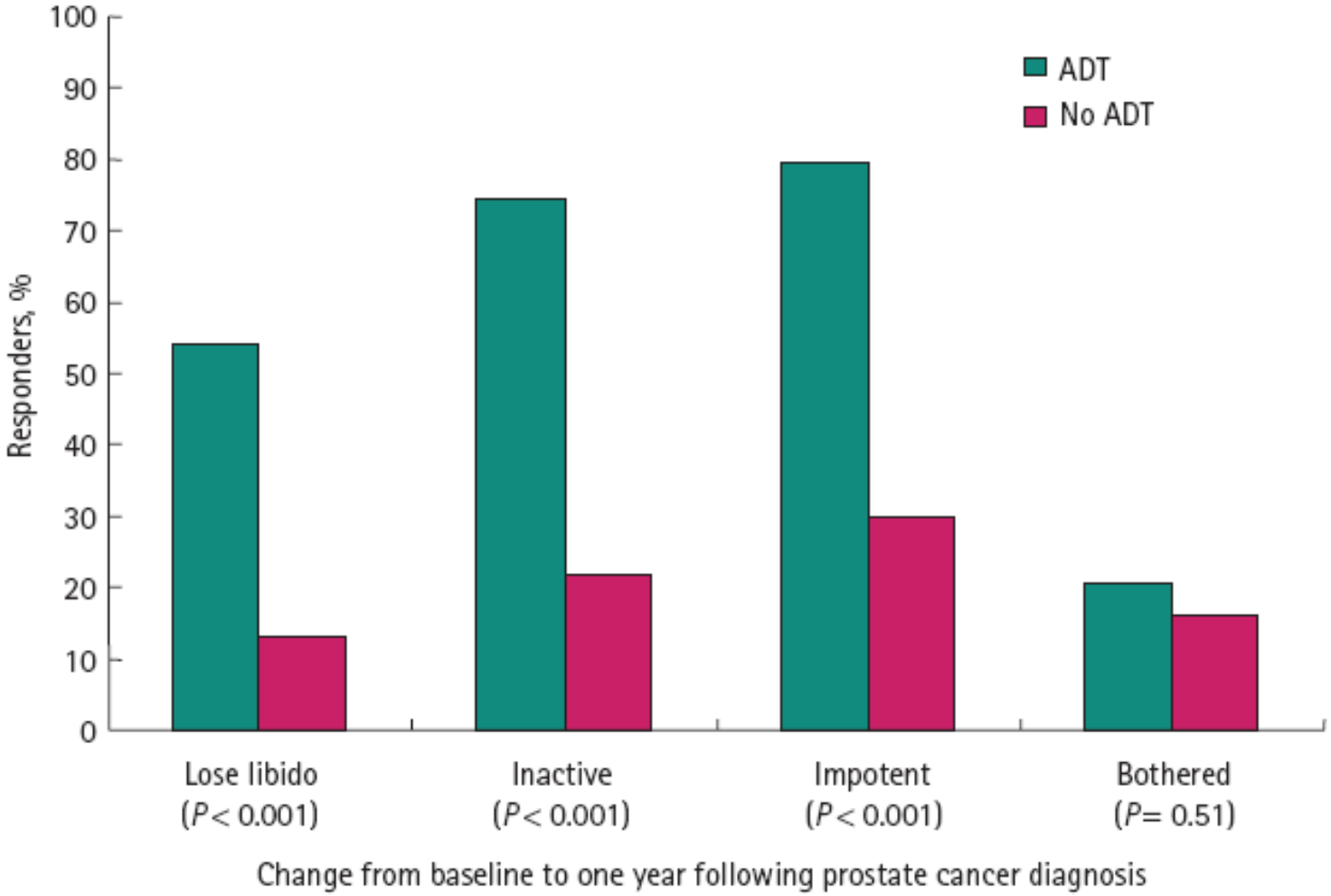
Sexual dysfunction - generally



Potosky et al. J Natl Cancer Inst 2000;92:1582-92

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Sexual dysfunction - treatment

- Phosphodiesterase Type 5 Inhibitors
  - In case of preserved libido
- Intraurethral/intracavernous Injections
- Protheses
- Counseling

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Hot flushes - generally

- Up to 75% of all men on ADT
- Mechanism:
  - Catecholamin-induced stimulation of the thermoregulatory centre in the hyopthalamus
- Thermal feeling, redness, sweating
  - Socially disturbing
- Sleep disorders – Fatigue
- Mostly not improving gradually

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Hot flushes – therapy

- Hormonal (cave progressive disease, side effects)
- Antidepressiva (13% mit Depression)
- Accupuncture: 1 small positive study
- Gabapentin
- Avoidance of:
  - Stress, coffeine, spicy meals, alcohol, heat

Gynecomastia - generally

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- Painful – socially disturbing
- Irreversible after 1 year (fibrosis)
- Incidence:
  - LHRH-Agonists/Orchiectomy:1-14%
  - Antiandrogenes mono: 43-85%
  - complete Androgene blockade : 13-22%
  - Oestrogenes: 40-80%
- Mechanism: Oestrogen/Androgen Ratio↑

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Gynecomastia - therapy

- Prophylaxis vs. Therapy
  - Prophylaxis in case of Anti-Androgene-Monotherapy!
- Radiotherapy
  - Prophylaxis: avoidance of Gynecomastia in up to 90% (6 – 12 Gy/1-3d)
  - Therapy: only pain control!
- Surgery
  - Subcutaneous mastectomy; Liposuction
- Oestrogene-Antagonists (Tamoxifen)

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Psychiatric und cognitive disorders

- Androgene-Rezeptors in the CNS
- Possible relationship for:
  - Depression
  - Disturbance of memory and concentration
- BUT:
  - Inconsistent data, also consider age, comorbidities or other causes (drugs, brain mets, thyroid function disorders)

Anemia

- Lack of Testosteron-driven stimulation of hematopoiesis
  - Starts after 1 month, lowest values after 6 months
- In 90% decrease Hb 10%; ca. 10-20g/L
- About 13% symptomatic (decrease Hb 25%)
- Optionally Epo (no data, not covered by insurance)

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Osteoporosis - generally

- ADT decreases bone mineral density (BMD)
  - BMD loss -4%/year for 2 years, -2% yearly thereafter
  - Testosterone prevents bone resorbtion
- Increased fracture risk with ADT
  - cumulative risk 15 years after orchiectomy 40% vs 19%
  - Risiko↑ mit length of time of ADT
- 29% Osteopenia, 5% Osteoporosis before start of ADT

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Osteoporosis – Prophylaxis/Therapy

- Risk assessment (low vs high)
  - High Risk:
    - ADT >6 months, family history, nicotine-/alcohol abusus, steroids, body weight ↓, comorbidities, history of fractures
- Baseline DEXA scan
- Lifestyle Changes
  - alcohol, no nicotine, training
- Vitamin D und Calcium Supplementation
  - e.g. Calcimagon® D3 (500mg Calcium , 400E Vit D): 1-2/d
  - Bisphosphonates if manifest Osteoporosis

Metabolic Syndrome - generally

- Definition:
  - ≥ 3 of 5 criteria
    - increased fasting-glucose > 6,2 mmol/l
    - increased Triglycerides ≥ 1,7 mmol/l
    - HDL cholesterine < 1,0 mmol/l
    - Blood pressure ≥ 130/85 mmHg
    - Hip size > 102cm
- Poor data but probable relationship
- Increased cardiovascular risk

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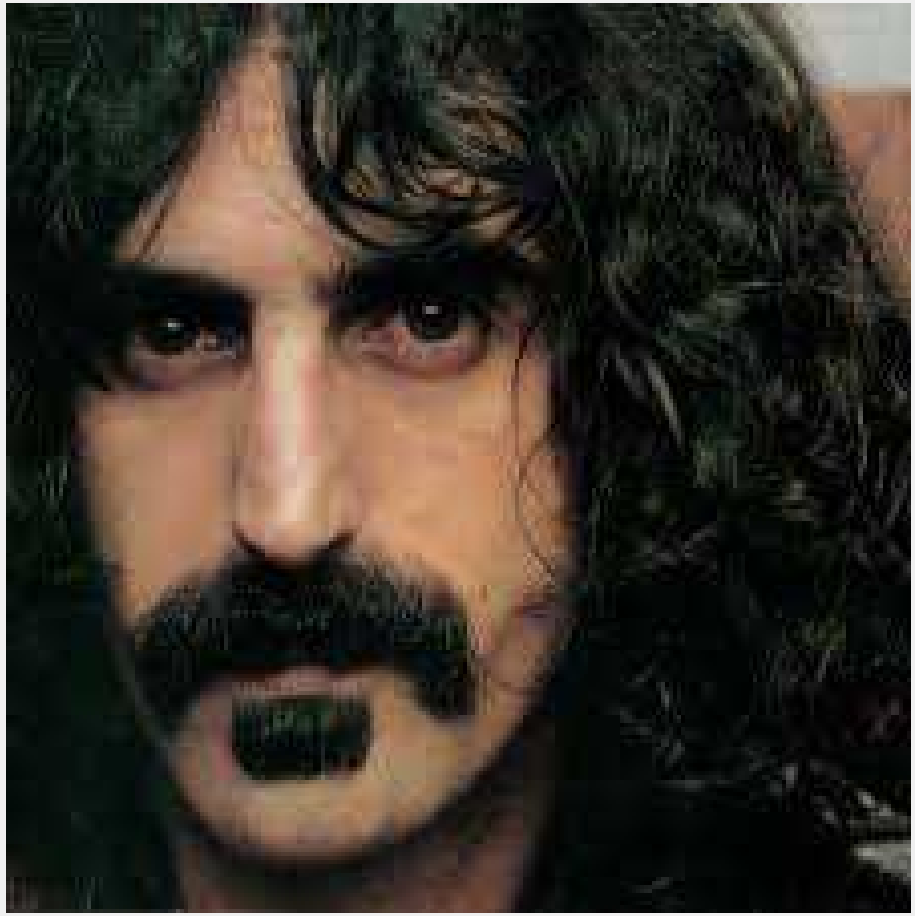

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