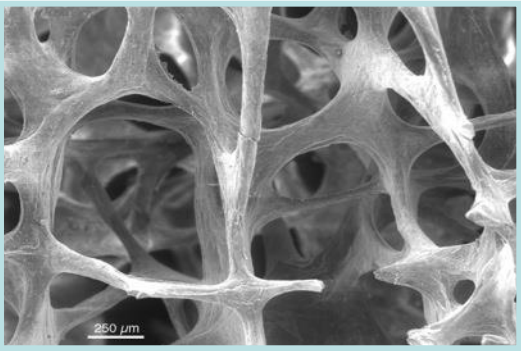
Wenn Knochen brechen



Elisabeth Zwettler
Ärztliche Direktorin Hanusch-Krankenhaus
Med. Leitung Gesundheitsverbund
Wiener Gebietskrankenkasse
Ludwig Boltzmann Institut für Osteologie

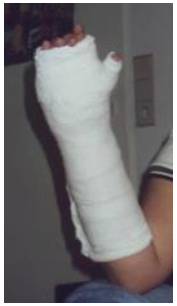
16.Oktober 2015

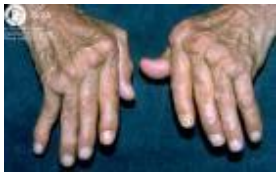
Wiener Gebietskrankenkasse WGKK GESUNDHEITSVERBUND

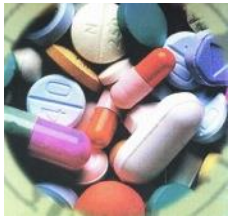
hanuschkrankenhaus GESUNDHEITSVERBUND

MEDIZINISCHE UNIVERSITÄT WIEN LEHRKRANKENHAUS

Osteoporoserisiko





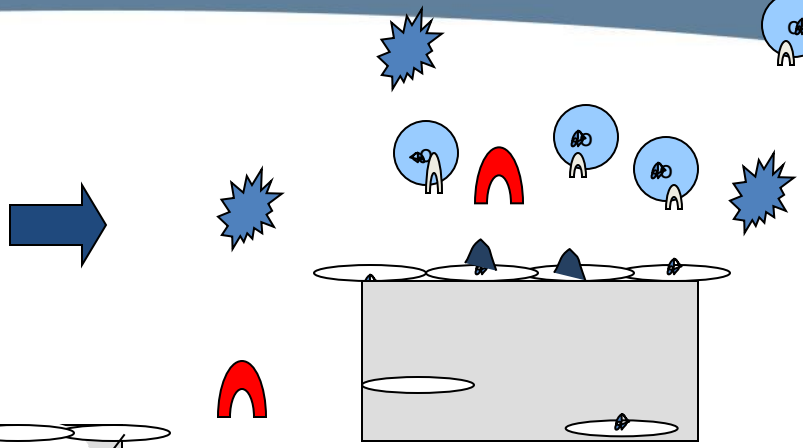


Inaktivitätsosteoporose

Bone remodeling

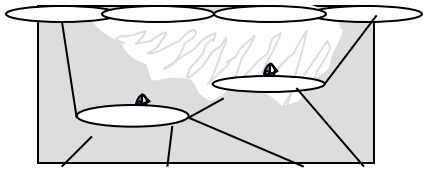
Osteoklastenvorläufer

Auslöser:
Zytokine,
Belastung



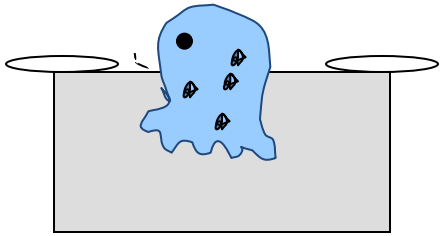
RANKL
Osteoprotegerin
RANK

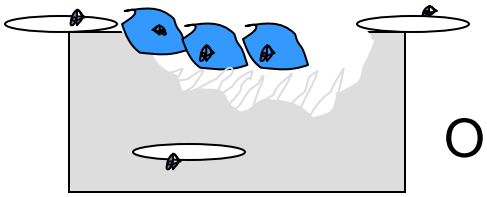
Lining cell



Osteozyt

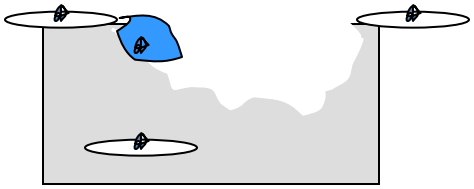
Osteoklast



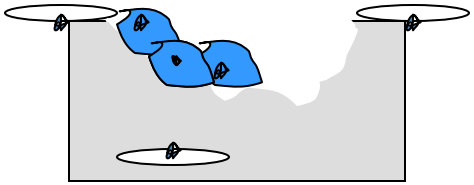


Osteoid

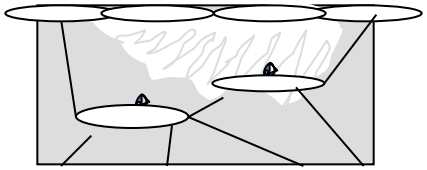
Osteoblast



Mineralisierung



Osteozyt



90-95 % der Knochenzellen

Knochenumbau (SOST-Sclerostin, RANK,
DMP-1- Dentin-Matrix- Protein-1)

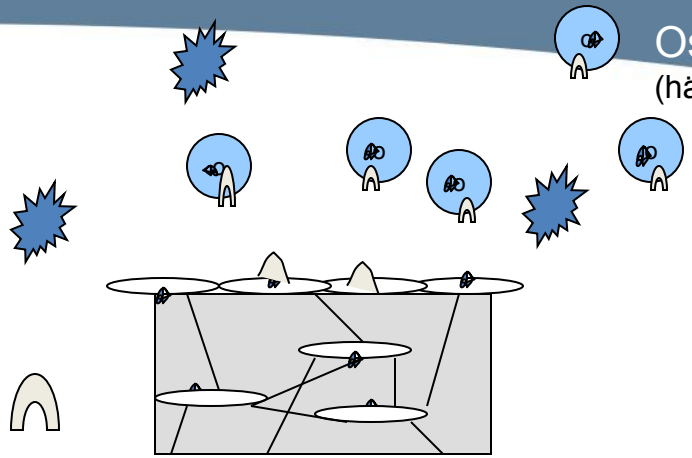
Mineralisierung

Phosphorstoffwechsel (FGF23, MEPE, PHEX)

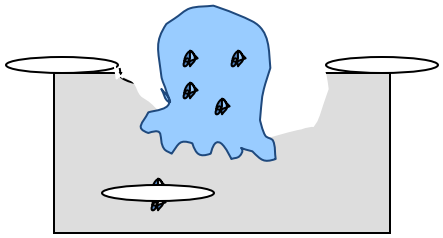
Lynda Bonewald. The Amazing Osteocyte.
Journal of Bone and Min Res. 2011(26) pp 229–238

Osteoklastenvorläufer
(hämatopoietische Stammreihe)

Auslöser:
Zytokine,
Belastung

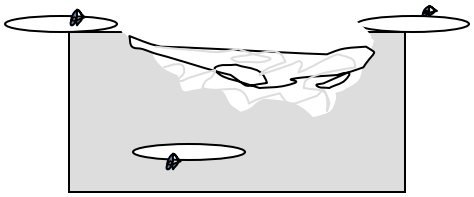


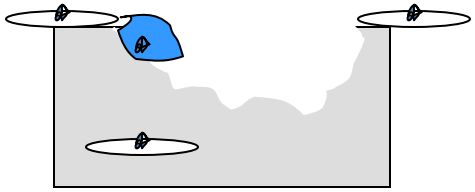
Osteozyten

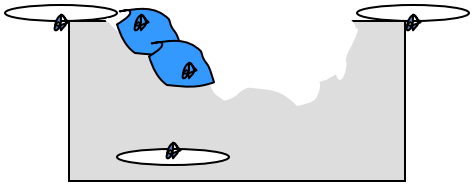


Immobilisation:
Abbau ↑
Aufbau ↓

Resorptionsmarker erhöht
nach 2 Tagen Immobilität







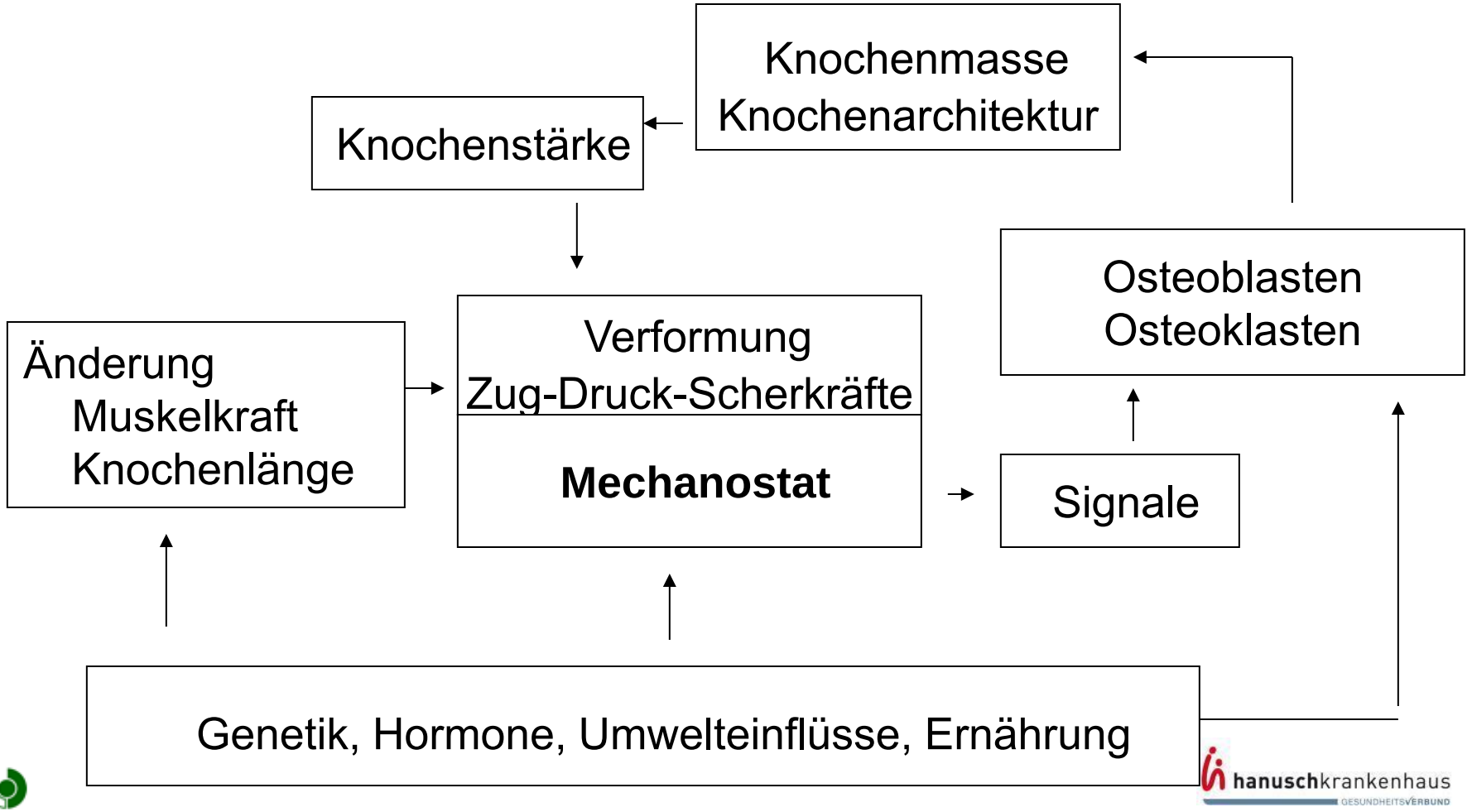
hanuschkrankenhaus
GESUNDHEITSVERBUND

Das Gesetz der Transformation der Knochen

Bei Änderung der statischen Beanspruchung durch Unfall oder Krankheit passt sich die Architektur des Knochen den neuen Verhältnissen an.

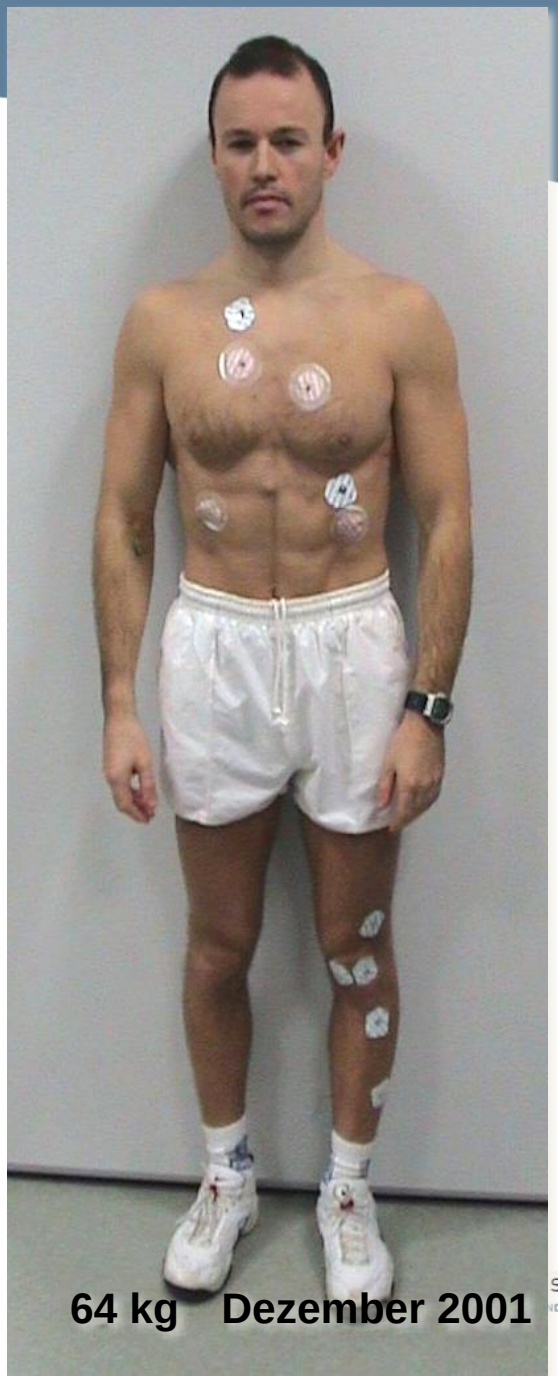
Julius Wolff, 1892

Mechanostathypothese
nach **Harald Frost**

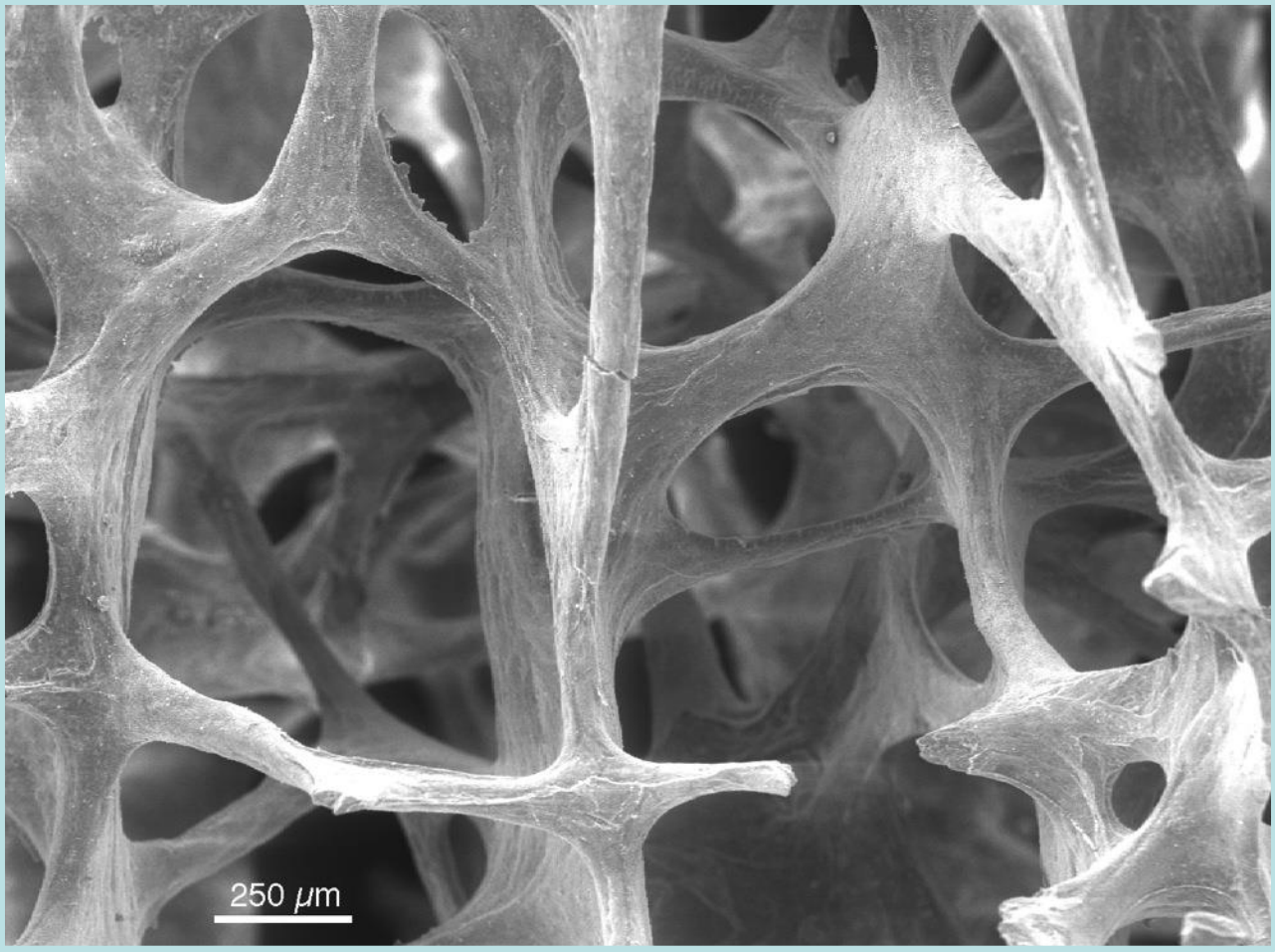


3 Monate
bed rest

Mit freundlicher Genehmigung
D. Felsenberg



Trabekulärer Knochen



Rasterelektronenmikroskop, Paul Roschger, LBIO

Apalliker Care Unit
Geriatriezentrum am Wienerwald

30 PatientInnen (14 Frauen, 16 Männer)
22-73 Jahre
4 Monate – 19 Jahre

22 PatientInnen osteoporotische Werte in DXA-Messung
6 PatientInnen osteopenische Werte
2 Patienten Normalwerte

1 Patientin ausreichender Vitamin D Status
29 PatientInnen erhöhte Knochenabbaumarker

SHORT REPORT

JBMR®

Low Bone Mineral Density and Fragility Fractures in Permanent Vegetative State Patients

Bastian Oppl,[1] Gabriele Michitsch,[2] Barbara Misof,[1] Stefan Kudlacek,[3] Johann Donis,[2] Klaus Klaushofer,[1] Jochen Zwerina,[1] and Elisabeth Zwettler[1]

[1]Ludwig Boltzmann Institute of Osteology at the Hanusch Hospital of WGKK and AUVA Trauma Centre Meidling, 1st Medical Department, Hanusch Hospital, Vienna, Austria

[2]Department of Neurology, Apallic Care Unit, Geriatric Centre Wienerwald, Vienna, Austria

[3]Department of Internal Medicine, Krankenhaus der Barmherzigen Brüder, Vienna, Austria

ABSTRACT

Disuse of the musculoskeletal system causes bone loss. Whether patients in vegetative state, a dramatic example of immobilization after severe brain injury, suffer from bone loss and fractures is currently unknown. Serum markers of bone turnover, bone mineral density (BMD) measurements, and clinical data were cross-sectionally analyzed in 30 consecutive vegetative state patients of a dedicated apallic care unit between 2003 and 2007 and compared with age- and sex-matched healthy individuals. Vegetative state patients showed low calcium levels and vitamin D deficiency compared with healthy controls. Serum bone turnover markers revealed high turnover as evidenced by markedly elevated carboxy-terminal telopeptide of type I collagen (β-crosslaps) and increased levels of alkaline phosphatase. BMD measured by dual-energy X-ray absorptiometry (DXA) scanning showed strongly decreased *T*- and *Z*-scores for hip and spine. Over a period of 5 years, 8 fragility fractures occurred at peripheral sites in 6 of 30 patients ($n = 3$ femur, $n = 2$ tibia, $n = 2$ fibula, $n = 1$ humerus). In conclusion, high bone turnover and low BMD is highly prevalent in vegetative state patients, translating into a clinically relevant problem as shown by fragility fractures in 20% of patients over a time period of 5 years.

KEY WORDS: VEGETATIVE STATE; BONE TURNOVER; IMMOBILIZATION; OSTEOPOROSIS; SCLEROSTIN

Diagnostik

bei

Fraktur ohne adäquates Trauma
Immobilität > 2 Monate ?

Anamnese

DXA, BWS-, LWS-Röntgen

Labor: Kalzium, Phosphor, Alkalische Phosphatase, Blutbild, Kreatinin, Gesamteiweiß, Gamma-GT, TSH, 25-OH-Vitamin D (Knochenumbaumarker, PTH, FSH, Testosteron, ...)

Knochendichtemessung mit DXA

T-Score bis –1,0 SD	Normal
T-Score < –1,0 SD bis –2,5 SD	Osteopenie
T-Score ab –2,5 SD	Osteoporose
T-Score ab –2,5 SD plus eine oder mehrere Frakturen	Manifeste Osteoporose

SD –Standard Deviation

WHO 1994

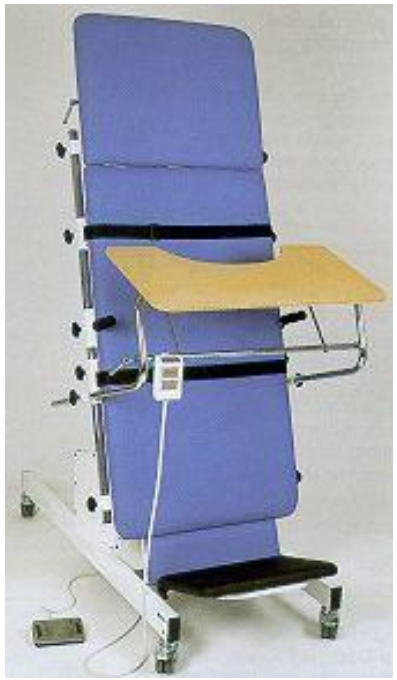
Allgemeine Therapiemaßnahmen

Lebensstilmaßnahmen

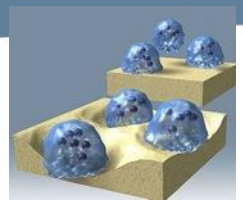
- Bewegung
- Ernährung

Basismedikation

- Kalziumzufuhr 800-1000mg pro Tag
- Vitamin D 1000-2000IE



Kudlacek S, Schneider B, Peterlik M.: Assessment of Vitamin D and Calcium status in healthy adult Austrians. Europ. J Clin. Invest. 2003; 33:323-331



Spezifische Therapie

Antiresorptiv

Bisphosphonate
(Alendronat, Risedronat
Ibandronat, Zoledronat)

Denosumab

SERMs (Raloxifen)

(Östrogen)

(Strontiumranelat)

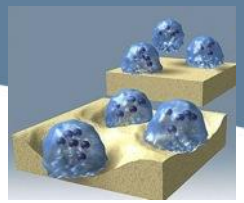
Anabol

Parathormon
(Parathormon,Teriparatide)

Pipeline

Odanacatib
(cathepsin-k AK)
Romosozumab
(anti-scerostin AK)

Bisphosphonat



Zoledronate
Aclasta®

Zulassung:

postmenopausale,

glucocorticoidinduzierte,

männliche Osteoporose

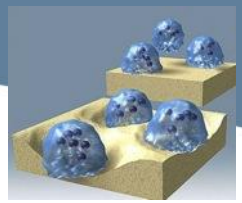
5mg in 100ml NaCl
über 15 Minuten
einmal /Jahr
mit Basistherapie
3 Jahre

NW!

Black D, Delmas, S, Eastell R, et al for the HORIZON Pivotal Fracture Trial. Once-Yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis. NEJM 2007; 356(18):1809-22.

Lyles KW et al. Zoledronic acid and clinical fractures and mortality after hip fracture. NEJM 2007; 357:1799-1809

RANKL- AK



Denosumab
Prolia ®
60mg

Zulassung:

postmenopausale Osteoporose

Prostataca mit hormonablativer Therapie

Injektion s.c. / 6Monate
mit Basistherapie

human monoclonal antibody that binds and neutralizes human RANKL

Cummings SR, et al. Twice Yearly Denosumab, a Monoclonal Antibody to RANK-ligand, for Prevention of Fractures in Postmenopausal Women with Osteoporosis. N Engl J Med, 2009 Aug. 20

Smith MR, et al. Denosumab for the Prevention of Bone Loss and Fractures in Men Receiving Androgen Deprivation Therapy in Non-Metastatic Prostate Cancer. N Engl J Med, 2009 Aug. 20

Allgemeine Therapiemaßnahmen

Frakturversorgung

Schmerztherapie

Mobilisierung

Physiotherapie

Ev. Orthesen

Ev. Kyphoplastie

http://www.dv-osteologie.org/dvo_leitlinien/osteoporose-leitlinie-2014

Vegetative state patients commonly suffer from low bone mineral density and fragility fractures

No clinical guidelines regarding prevention, diagnosis and therapy

Current literature

- Early and sustained administration of **bisphosphonates** attenuated rate of bone loss until steady state between osteogenic and osteolytic activites was reached. Chang et al, 2013
-
- Early treatment with **denosumab** increased lumbar and femoral bone mineral density in 14 individuals with spinal cord injury. Gifre et al, 2015

- **Sclerostin antibody** prevented bone loss in rodent spinal chord injury model. Beggs et al, 2014

Inaktivität

Knochenmasseverlust

rasch und ausgeprägt (lokal und generalisiert)

Basismaßnahmen

Bewegungstraining (Mobilisierung!)

ausreichender Kalzium- und Vitamin D Status

Osteoporosediagnostik

Spezifische Osteoporosetherapie (off label, Nebenwirkungen).

Dauer: kurzfristig - 5Jahre?