



# Volba typu anestézie na prognózu onkologicky nemocných

D. Mach  
Nové Město na Moravě





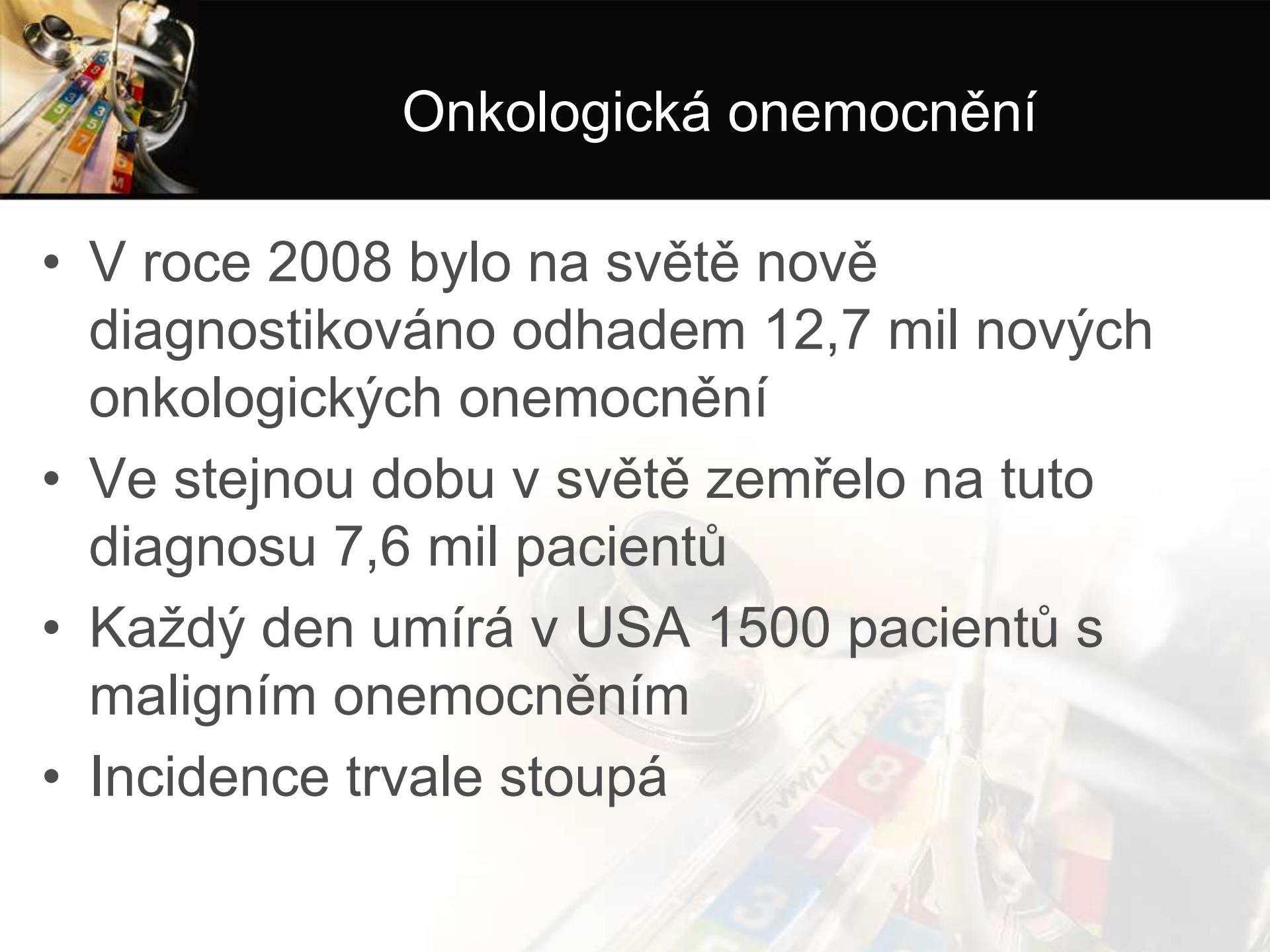


# Expanding our horizons

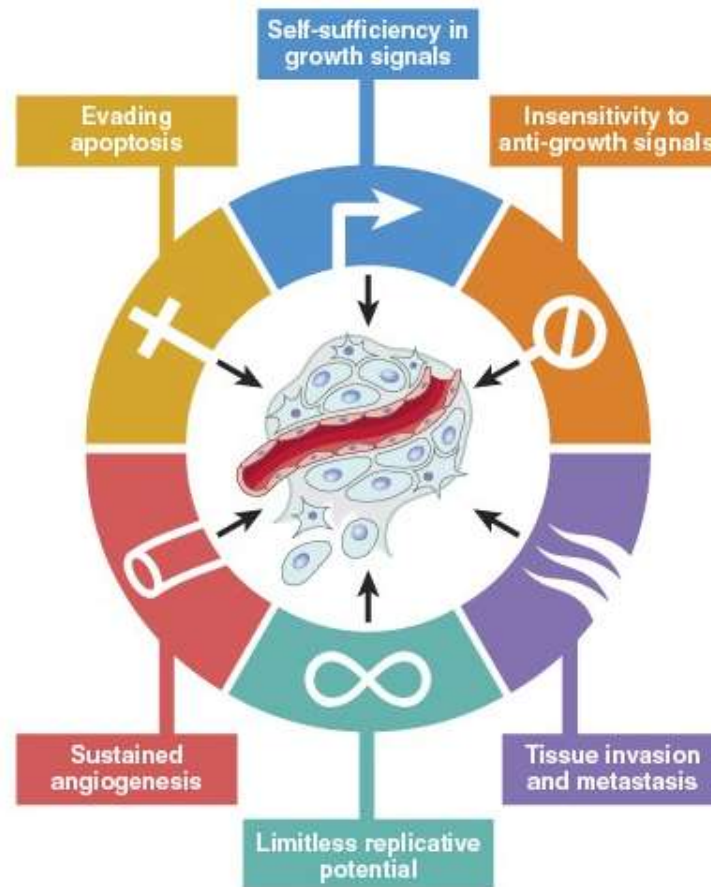




# Onkologická onemocnění

- V roce 2008 bylo na světě nově diagnostikováno odhadem 12,7 mil nových onkologických onemocnění
  - Ve stejnou dobu v světě zemřelo na tuto diagnosu 7,6 mil pacientů
  - Každý den umírá v USA 1500 pacientů s maligním onemocněním
  - Incidence trvale stoupá
- 

# Patogeneze nádorových onemocnění

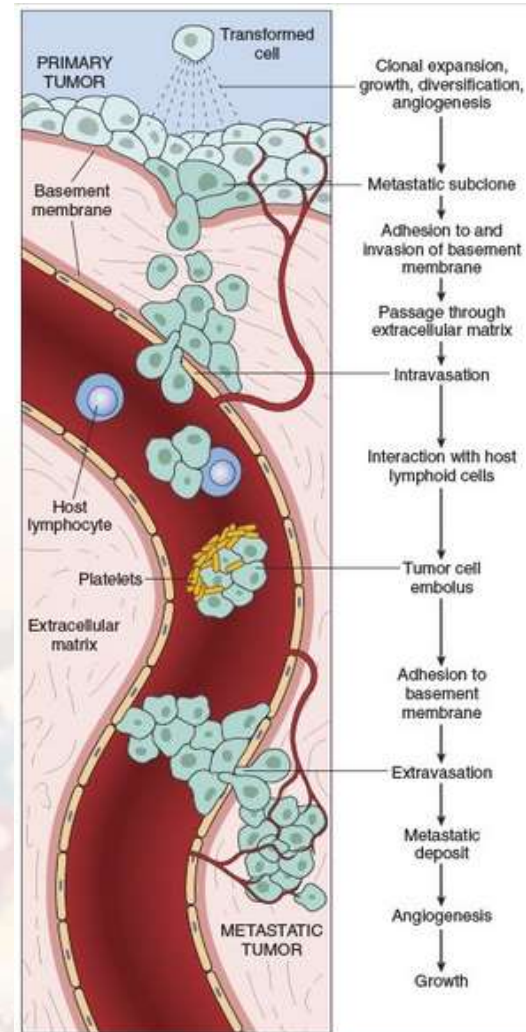


**Figure 6-17**

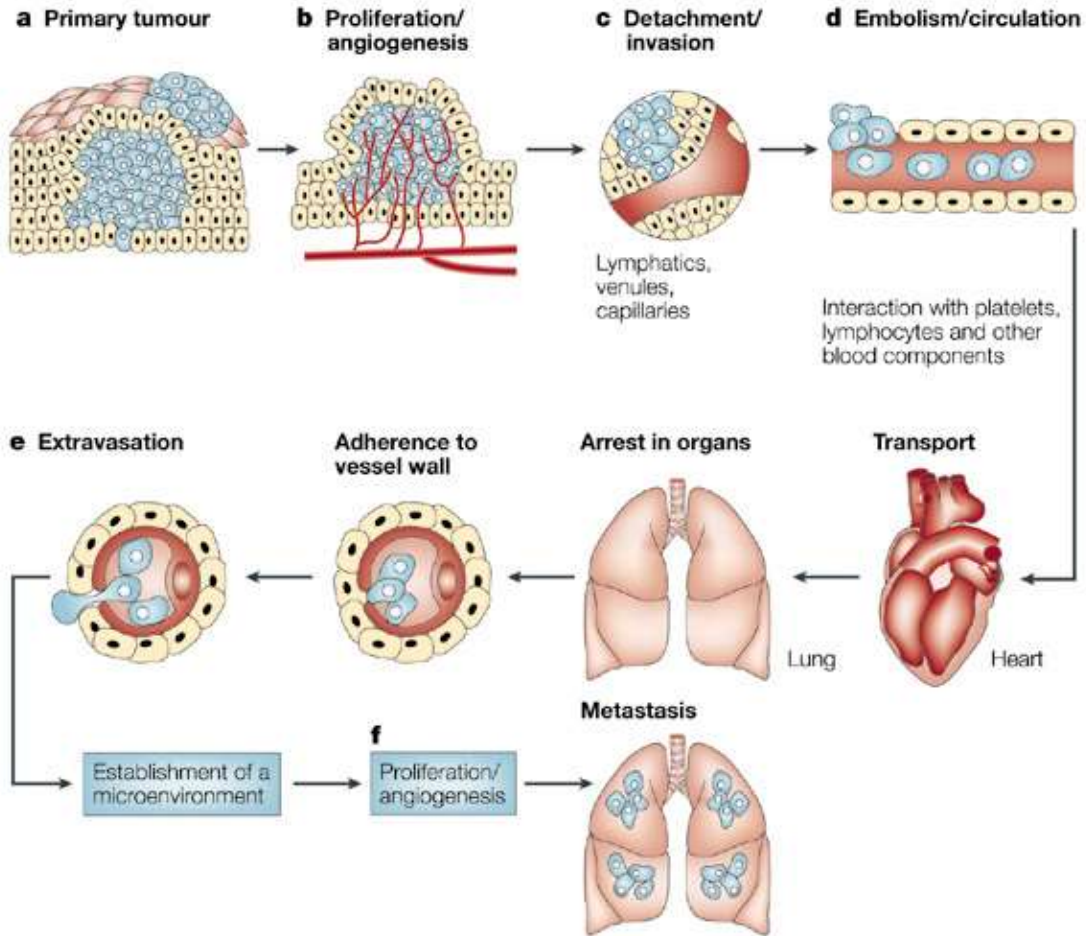
Six hallmarks of cancer. Most cancer cells acquire these properties during their development, typically by mutations in the relevant genes. (From Hanahan D, Weinberg RA: The hallmarks of cancer.

# Patogeneze metastáz

- Metastázování je komplexní proces zahájený uvolněním nádorových buněk z primárního nádoru
- Jen méně než 0,1% uvolněných buněk je vitálních déle než 24 hodin
- Podmínkou je překonání imunitního systému a rychle zahájená angiogeneze
- Podpořena uvolněním proangiogenních faktorů VEGF, PGE2.....HIF1alfa
- Existují specifické subpopulace makrofágů rozeznávajících nádorové buňky CD11b+ (meta tu prsu)

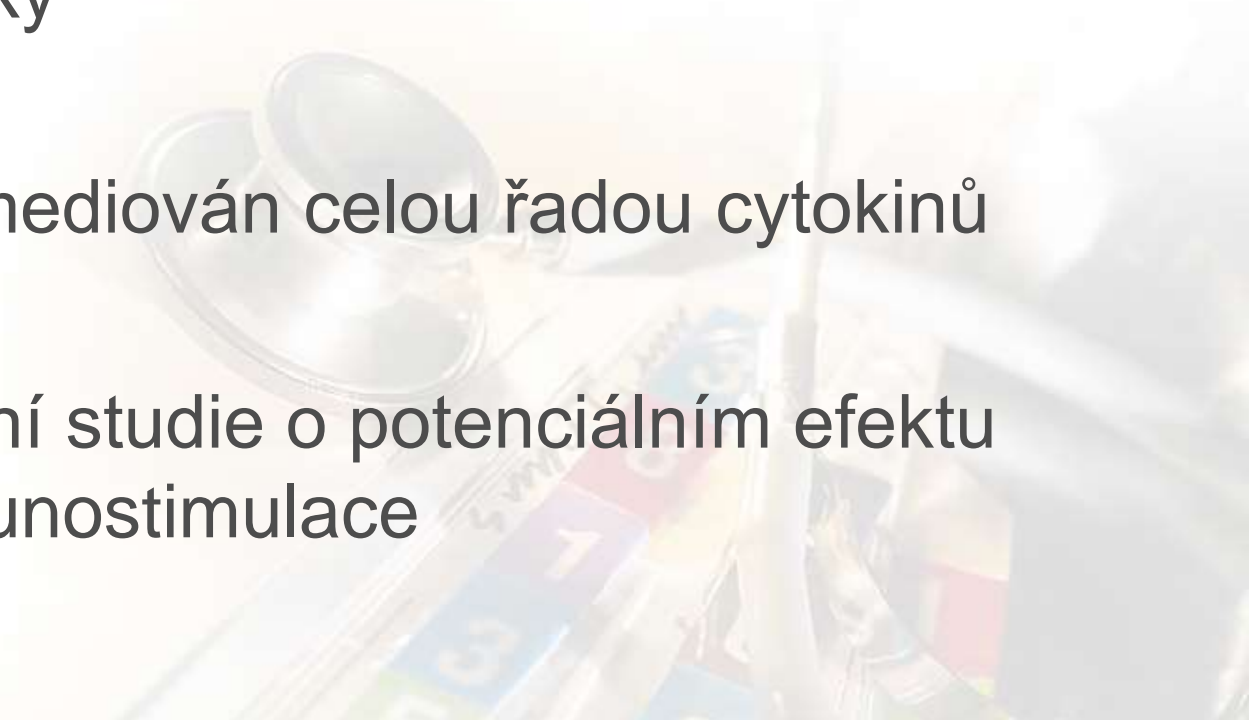


# Patogeneze metastáz



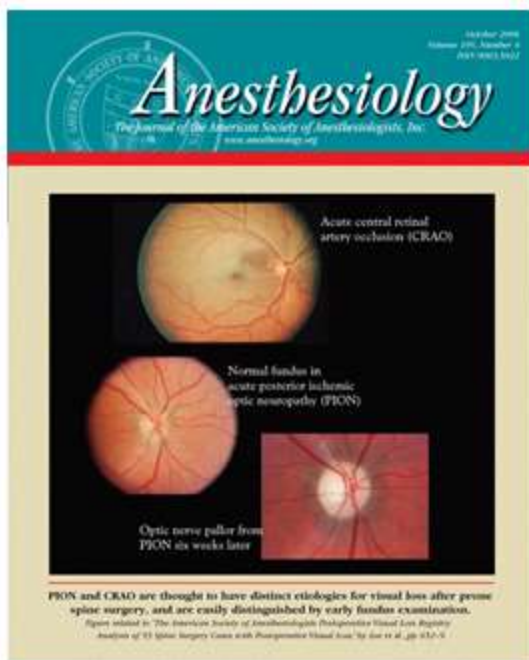


# Přirozená protinádorová imunita

- Natural killer cells (NK)
  - Cytotoxic T cells
  - Mononukleáry
  - Dendritické buňky
  
  - Celý proces je mediován celou řadou cytokinů
  
  - Existují i animální studie o potenciálním efektu perioperační imunostimulace
- 



# Vliv anestézie na prognózu onkologicky nemocných



FREE

Clinical Science | October 2006

## Can Anesthetic Technique for Primary Breast Cancer Surgery Affect Recurrence or Metastasis?

Aristomenis K. Exadaktylos, M.D.; Donal J. Buggy, M.D., M.Sc., D.M.E., F.R.C.P.I., F.C.A.R.C.S.I., F.R.C.A.; Denis C. Moriarty, F.C.A.R.C.S.I.; Edward Mascha, Ph.D.; Daniel I. Sessler, M.D., Ph.D.

# Vliv anestézie na prognózu onkologicky nemocných

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doi:10.1093/bja/aeu261

## EDITORIAL

### Special issue on anaesthesia and cancer

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# Efekt perioperačních aktivit na možné metastazování

**Table 1** How perioperative factors could potentially influence cancer recurrence and metastasis

Surgery	Stimulates neuroendocrine and cytokine stress response Suppresses cell-mediated immunity Disperses tumour 'emboli' Promotes tumour growth and metastasis in animal models
Pain	Animal studies indicate that inadequately treated postoperative pain suppresses NK cell activity and promotes metastasis
Volatile anaesthesia	Possibly alters the activity of leucocytes Associated with induction of apoptosis in lymphocytes <i>in vitro</i>
Propofol	Attenuates cancer cell migration, proliferation, and metastasis <i>in vitro</i> Possible COX inhibitor
Opioids	MORs are over-expressed in certain cancers Inhibit cell-mediated and humoral immunity Promote tumour cell migration, proliferation, and cancer gene expression in human cells <i>in vitro</i> Facilitate angiogenesis
NSAIDs/COX inhibitors	COX over-expressed in many cancers PGs inhibit NK cell cytotoxicity and modulate the tumour microenvironment Long-term use associated with reduced incidence of cancer
Allogeneic blood transfusion	Associated with immunosuppression, increased risk of cancer recurrence, and reduced survival
Psychological stress	Animal and clinical evidence of an association between stress, depression, and cancer progression Activates HPA-axis and sympathetic nervous system Contributes to perioperative immunosuppression
Hypothermia	Stimulates sympathetic nervous system and glucocorticoid release Increases bleeding and allogeneic blood transfusion Suppresses cell-mediated and humoral immunity



# Efekt morfinu na progresi nádoru prsu

*British Journal of Anaesthesia* 113 (S1):i4–i13 (2014)  
Advance Access publication 26 May 2014 · doi:10.1093/bja/aeu090

BJA

## Morphine stimulates cancer progression and mast cell activation and impairs survival in transgenic mice with breast cancer

J. Nguyen<sup>1</sup>, K. Luk<sup>1</sup>, D. Vang<sup>1</sup>, W. Soto<sup>1</sup>, L. Vincent<sup>1</sup>, S. Robiner<sup>1</sup>, R. Saavedra<sup>1</sup>, Y. Li<sup>1</sup>, P. Gupta<sup>1,2</sup> and K. Gupta<sup>1\*</sup>

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# Protinádorový efekt lokálních anestetik

*British Journal of Anaesthesia* **113** (S1): i32–i38 (2014)  
Advance Access publication 19 June 2014 · doi:10.1093/bja/aeu201

BJA

## Lidocaine and ropivacaine, but not bupivacaine, demethylate deoxyribonucleic acid in breast cancer cells *in vitro*

P. Lirk<sup>1\*</sup>, M. W. Hollmann<sup>1</sup>, M. Fleischer<sup>2</sup>, N. C. Weber<sup>1</sup> and H. Fiegl<sup>2\*</sup>

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*British Journal of Anaesthesia* **113** (S1): i39–i48 (2014)  
Advance Access publication 22 May 2014 · doi:10.1093/bja/aeu104

BJA

## Potent inhibition by ropivacaine of metastatic colon cancer SW620 cell invasion and Na<sub>v</sub>1.5 channel function

D. T. Baptista-Hon<sup>1</sup>, F. M. Robertson<sup>1</sup>, G. B. Robertson<sup>1</sup>, S. J. Owen<sup>1</sup>, G. W. Rogers<sup>1</sup>, E. L. Lydon<sup>1</sup>,  
N. H. Lee<sup>2</sup> and T. G. Hales<sup>1,2\*</sup>

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# Vliv epidurální anestézie na angiogenezi

*British Journal of Anaesthesia* 113 (S1): i49–i55 (2014)

Advance Access publication 25 June 2014 · doi:10.1093/bja/aeu148

BJA

## Effect of thoracic epidural anaesthesia on serum vascular endothelial growth factor C and cytokines in patients undergoing anaesthesia and surgery for colon cancer

Y. J. Xu<sup>1,2†</sup>, W. K. Chen<sup>1,2†</sup>, Y. Zhu<sup>1,2</sup>, S. L. Wang<sup>1,2</sup> and C. H. Miao<sup>1,2\*</sup>

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# Vliv typu anestézie na aktivitu NKC

*British Journal of Anaesthesia* 113 (S1): i56–i62 (2014)  
Advance Access publication 9 July 2014 · doi:10.1093/bja/aeu200

BJA

## Effect of anaesthetic technique on the natural killer cell anti-tumour activity of serum from women undergoing breast cancer surgery: a pilot study

A. Buckley<sup>1\*</sup>, S. McQuaid<sup>2</sup>, P. Johnson<sup>2</sup> and D. J. Buggy<sup>1,3,4</sup>

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# Vliv typu anestézie na nádorovou apoptózu

British Journal of Anaesthesia 113 (S1): i63–i67 (2014)  
Advance Access publication 9 July 2014 · doi:10.1093/bja/aet581

BJA

## Differential effects of serum from patients administered distinct anaesthetic techniques on apoptosis in breast cancer cells *in vitro*: a pilot study

A. I. Jaura<sup>1,2</sup>, G. Flood<sup>1,2</sup>, H. C. Gallagher<sup>2</sup> and D. J. Buggy<sup>1,2,3,4\*</sup>

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<sup>2</sup> School of Medicine and Medical Science, Conway Institute, University College Dublin, Belfield, Dublin 4, Ireland

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<sup>4</sup> Department of Outcomes Research, Cleveland Clinic, Cleveland, OH, USA





# Protektivní efekt NSAID?

*British Journal of Anaesthesia* 113 (S1): i82–i87 (2014)

Advance Access publication 23 January 2014 · doi:10.1093/bja/aet464

BJA

## **Intraoperative use of ketorolac or diclofenac is associated with improved disease-free survival and overall survival in conservative breast cancer surgery**

P. Forget<sup>1\*</sup>, C. Bentin<sup>2</sup>, J.-P. Machiels<sup>3</sup>, M. Berliere<sup>2</sup>, P. G. Coulie<sup>4</sup> and M. De Kock<sup>1</sup>

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<sup>4</sup> de Duve Institute, Université catholique de Louvain, Brussels, Belgium

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# Expresse MOR u primárního tumoru a meta

*British Journal of Anaesthesia* 113 (S1): i103–i108 (2014)  
Advance Access publication 11 June 2014 · doi:10.1093/bja/aeu165

BJA

## Increased $\mu$ -opioid receptor expression in metastatic lung cancer

P. A. Singleton<sup>1,2\*</sup>, T. Mirzapoiazova<sup>1</sup>, R. Hasina<sup>1,3</sup>, R. Salgia<sup>3</sup> and J. Moss<sup>2</sup>

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# Vliv neuroaxiální analgezie po RAPE

*British Journal of Anaesthesia* 113 (S1):i95–i102 (2014)

Advance Access publication 16 December 2013 · doi:10.1093/bja/aet467

BJA

## Association between neuraxial analgesia, cancer progression, and mortality after radical prostatectomy: a large, retrospective matched cohort study

F. Scavonetto<sup>1†</sup>, T. Y. Yeoh<sup>1,4†</sup>, E. C. Umbreit<sup>2</sup>, T. N. Weingarten<sup>1</sup>, M. T. Gettman<sup>2</sup>, I. Frank<sup>2</sup>, S. A. Boorjian<sup>2</sup>, R. J. Karnes<sup>2</sup>, D. R. Schroeder<sup>3</sup>, L. J. Rangel<sup>3</sup>, A. C. Hanson<sup>3</sup>, R. E. Hofer<sup>1</sup>, D. I. Sessler<sup>5</sup> and J. Sprung<sup>1\*</sup>

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# Negativní vliv hyperoxemie?

*British Journal of Anaesthesia* 113 (S1): i74–i81 (2014)  
Advance Access publication 23 May 2014 · doi:10.1093/bja/aeu110

BJA

## Risk of new or recurrent cancer after a high perioperative inspiratory oxygen fraction during abdominal surgery

C. S. Meyhoff<sup>1\*</sup>, L. N. Jorgensen<sup>2</sup>, J. Wetterslev<sup>3</sup>, V. D. Siersma<sup>5</sup> and L. S. Rasmussen<sup>4</sup> PROXI Trial Group

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<sup>2</sup> Digestive Disease Center, Bispebjerg Hospital, University of Copenhagen, Bispebjerg Bakke 23, DK-2400 Copenhagen NV, Denmark

<sup>3</sup> Copenhagen Trial Unit, Centre for Clinical Intervention Research and <sup>4</sup> Department of Anaesthesia, Centre of Head and Orthopaedics, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK-2100 Copenhagen Ø, Denmark


<sup>5</sup> The Research Unit for General Practice and Section of General Practice, Department of Public Health, University of Copenhagen, Øster Farimagsgade 5, DK-1014 Copenhagen K, Denmark



# Vliv hypotermie?

## Intraoperative Hypothermia During Cytoreductive Surgery for Ovarian Cancer and Perioperative Morbidity

*Mehdi Moslemi-Kebria, MD, Sherif A. El-Nashar, MBBCh, MS, Giovanni D. Aletti, MD,  
and William A. Cliby, MD*

- 146 pacientek
  - Hypotermie definována teplotou pod 36 stC
  - Rozdíl v přežívání 34 versus 45 měsíců
- 



# Vliv allogení krevní transfuze?

[J Thorac Cardiovasc Surg](#). 2012 Apr;143(4):815-9. doi: 10.1016/j.jtcvs.2011.12.031. Epub 2012 Feb 9.

**Leukocyte-depleted blood transfusion is associated with decreased survival in resected early-stage lung cancer.**

[Ng T<sup>1</sup>](#), [Ryder BA](#), [Chern H](#), [Sellke FW](#), [Machan JT](#), [Harrington DT](#), [Cioffi WG](#).

[Ann Surg Oncol](#). 2008 Jan;15(1):34-45. Epub 2007 Oct 18.

**Anemia and transfusions in patients undergoing surgery for cancer.**

[Weber RS<sup>1</sup>](#), [Jabbour N](#), [Martin RC 2nd](#).

[Interact Cardiovasc Thorac Surg](#). 2012 Jan;14(1):85-90. doi: 10.1093/icvts/ivr025. Epub 2011 Nov 15.

**Does blood transfusion increase the chance of recurrence in patients undergoing surgery for lung cancer?**

[Churchhouse AM<sup>1</sup>](#), [Mathews TJ](#), [McBride OM](#), [Dunning J](#).

# Dosavadní RETROSPEKTIVNÍ studie

**Table 2** Summary of retrospective clinical evidence of effects of regional anaesthesia and cancer recurrence. PVAA, paravertebral anaesthesia and analgesia

Type of study	Reference	Surgery	Technique	Outcome
Retrospective	Exadaktylos <i>et al.</i> 2006 <sup>86</sup>	Mastectomy and axillary clearance for breast cancer	GA+PVAA (n=50) GA+opioid analgesia (n=79)	4-fold decrease in cancer recurrence in PVAA group 2.5–4 yr follow-up
Retrospective	Biki <i>et al.</i> 2008 <sup>87</sup>	Radical prostatectomy for prostate carcinoma	GA+thoracic epidural analgesia (n=102) GA+opioid analgesia (n=123)	57% reduction in cancer recurrence in epidural group, P=0.012 Recurrence defines as increase in PSA
Retrospective	Wuethrich <i>et al.</i> 2010 <sup>88</sup>	Radical prostatectomy for localized prostate carcinoma	GA+thoracic epidural (n=103) GA+ketorolac+opioid analgesia (n=158)	Increase in clinical progression-free survival (P=0.009) in epidural group No difference in biochemical recurrence-free survival (P=0.42), cancer-specific survival (P=0.9), or overall survival (P=0.9)
Retrospective	Ishmail <i>et al.</i> 2011 <sup>89</sup>	Brachytherapy for cervical cancer	Neuraxial anaesthesia (n=69) GA (n=63)	No difference in tumour recurrence (P=0.526) or survival (P=0.537)
Retrospective	Gottschalk <i>et al.</i> 2010 <sup>90</sup>	Open colectomy	GA+epidural group (n=256) GA+opioid analgesia (n=253)	No difference in cancer recurrence except in patients >64 yr

# Dosavadní RETROSPEKTIVNÍ studie

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Retrospective	Gottschalk et al. 2010 <sup>90</sup>	Open colectomy	GA+epidural group (n=256) GA+opioid analgesia (n=253)	No difference in cancer recurrence except in patients >64 yr Follow-up 1.8 yr
Retrospective	Gupta et al. 2011 <sup>91</sup>	Open colectomy	GA+epidural (n=562) GA+PCA opioid analgesia (n=93)	GA+opioid group had higher mortality rate in rectal cancer (P=0.049) No difference with colon cancer (P=0.23)



# Dosavadní RETROSPEKTIVNÍ studie

Retrospective	Lin <i>et al.</i> 2011 <sup>92</sup>	Laparotomy for ovarian carcinoma	Epidural anaesthesia+analgesia (n=106) GA+opioid analgesia (n=37)	Epidural group had improved 3 yr and 5 yr survival rates (P=0.043)
Retrospective	De Oliveira <i>et al.</i> 2011 <sup>93</sup>	'Debulking' surgery for ovarian cancer	Epidural (n=55) Opioid analgesia (n=127)	Intraoperative epidural analgesia associated with reduced risk of cancer recurrence
Retrospective	Lai <i>et al.</i> 2012 <sup>94</sup>	Radiofrequency ablation of hepatocellular carcinoma	Epidural or GA hazard ratio for disease-free survival=3.66, P=0.001	GA associated with increased recurrence-free survival No difference in overall survival
Retrospective	Day <i>et al.</i> 2012 <sup>95</sup>	Laparoscopic colorectal resection for adenocarcinoma	Epidural (n= 07) Spinal (n=144) Morphine PCA (n=173)	No difference in overall (P=0.622) or disease-free survival at 5 yr (P=0.490)
Retrospective	Gottschalk <i>et al.</i> 2012 <sup>96</sup>	Lymph node dissection for malignant melanoma	Spinal anaesthesia (n=52) GA-sevoflurane/sufentanil (n=118) GA-propofol/remifentanil total i.v. anaesthesia (n=103)	Non-significant trend towards improved cumulative survival rate in spinal anaesthesia group (P=0.087)
RCT (follow-up)	Christopherson <i>et al.</i> 2008 <sup>97</sup>	Open colectomy for colorectal cancer	GA+epidural analgesia (n=85) GA+opioid analgesia (n=95)	Early survival benefit (for up to 1.46 yr) in epidural group (P=0.012) No benefit if metastatic disease present

# Dosavadní RETROSPEKTIVNÍ studie

Type of study	Reference	Surgery	Technique	Outcome
RCT (follow-up)	Tsui <i>et al.</i> 2010 <sup>98</sup>	Radical prostatectomy	GA+epidural analgesia (n=49) GA+opioid analgesia (n=50)	No difference in disease-free survival (P=0.44) 4.5 yr follow-up
RCT (follow-up)	Myles <i>et al.</i> 2011 <sup>79</sup>	Major abdominal surgery, subgroup analysis of patients with colorectal cancer	GA+epidural analgesia (n=230) GA+opioid analgesia (n=216)	No difference in cancer recurrence (P=0.61) or recurrence-free survival (P=0.61) Recurrence and mortality rates at 5 yr also similar
Retrospective population	Cummings <i>et al.</i> 2012 <sup>99</sup>	Open colectomy for non-metastatic colorectal cancer	Epidural analgesia (n=9670) Opioid pain management n=32 481	61% 5-yr survival with epidural vs 55% opioid (P<0.001) No difference in cancer recurrence rates (P=0.28)

# V současné době probíhající studie

**Table 3** The future: summary of some ongoing prospective, randomized, clinical trials by Outcomes Research Consensus

Title	Study design	Intervention	Primary outcome
Regional anaesthesia and breast cancer recurrence, NCT00418457	Multi-centre prospective randomized clinical trial, n= 1100	GA + postoperative opioid analgesia or GA or deep sedation with epidural or paravertebral anaesthesia/analgesia	Cancer recurrence rate up to 10 yr
The effect of adding intraoperative regional anaesthesia on cancer recurrence in patients undergoing lung cancer resection, NCT011799308	Prospective randomized, double-blind trial, n= 1532	GA + postoperative opioid analgesia or GA + thoracic epidural analgesia	Disease-free survival up to 5 yr
Regional anaesthesia in colon rectal surgery, NCT00684229	Multi-centre, prospective, randomized, double-blind trial, n= 2500	GA (sevoflurane) + opioid analgesia or GA + epidural anaesthesia/analgesia	Cancer recurrence rate up to 5 yr



# Existuje nějaké doporučení?

## Consensus statement from the *BJA* Workshop on Cancer and Anaesthesia

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<sup>8</sup> Department of Anaesthesiology, Intensive Care and Pain Medicine, University Hospital Muenster, Albert-Schweizer-Campus 1, Muenster 48149, Germany

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Děkuji za pozornost

