

Family, first name: Djonov Valentin G.

ORCID: 0000-0002-5062-1169

Date of birth: March 23rd, 1961 in Vidin, Bulgaria

Nationality: Bulgarian/Swiss

Web site: [https://www.ana.unibe.ch/research/topographic and clinical anatomy/](https://www.ana.unibe.ch/research/topographic%20and%20clinical%20anatomy/)

Academic degree: Doctor of Medicine and Professor of Anatomy, Histology and Embryology; University of Bern, Switzerland

Education:

2002 Habilitation – Anatomy, Histology and Embryology, University of Bern, Switzerland

1998 Doctor of Medicine, Faculty of Medicine, University of Bern, Switzerland

1987 Doctor of Medicine, Medical Academy, Sofia, Bulgaria

1981-1987 Medical Studies, Medical Academy, Sofia, Bulgaria

Current position:

2010 - until now Full Anatomy Professor /Director, Institute of Anatomy, University of Bern, Bern, Switzerland

Previous positions:

2007-2010 Full professor and Co-director, Institute of Anatomy, University of Fribourg, Fribourg, Switzerland

2006-2007 Associate Professor of Anatomy, Histology and Embryology, Institute of Anatomy, University of Bern, Switzerland

2003-2006 Assistant Professor (Dozent I), Institute of Anatomy, Bern, Switzerland

2001 - 2002 Lecturer, Institute of Anatomy, University of Bern, Bern, Switzerland

1995 – 2000 Research fellow, Institute of Anatomy, Bern, Switzerland

1995 -1995 Medical Assistant, Clinic of Urology, Inselspital, Bern, Switzerland

1992-1995 Research assistant, Department of Clinical Research, University of Bern

1991-1992 Medical Assistant, Regional Hospital, Herzogenbuchsee, Switzerland

1988-1990 Medical Assistant, Institute of Anatomy, University of Sofia, Bulgaria

1987-1988 General Practitioner, Hospital Vidin, Bulgaria

Fellowships and Awards:

2022: Doctor honoris causa from Medical University Sofia, Bulgaria

2021: Honorary citizen- City of Vidin, Bulgaria

2020: "Golden Laurel Branch" – the highest award of the Bulgarian foreign ministry for the development of Swiss-Bulgarian relationship in the field of medicine and bio-medical science.

2019: "Doctor of the Year" in Bulgaria for the development of Swiss-Bulgarian scientific connections and charity projects.

2007: Lady Davis Fellowship, Hebrew University, Jerusalem, Israel

2003: Teacher of the Year, University of Bern.

2001: Award of the Swiss Society of Anatomy, Histology and Embryology CHF 5'000.-

2001: Young Investigator Award University of Bern, San Salvatore Foundation, CHF 40'000.-

Supervision of graduate students and postdoctoral fellows:

Former PostDocs from my lab continuing their academic carrier as PIs (Last 10 years):

PD Dr. Ruslan Hlushchuk - University of Bern, Switzerland; Ass. Prof. Vladislav Volarevic - University of Kragujevac, Serbia; Ass. Prof. Oliver Baum - Charite-Universitätsmedizin Berlin, Germany; Ass. Prof. Ivanka Dimova - Medical Academy, Sofia, Bulgaria; Ass. Prof. Johannes Bastian - University of Bern, Switzerland; Ass. Prof. Andrey Makanya - University of Nairobi, Kenya; Ass. Prof. Nikolay Velinov - Medical Academy, Sofia, Bulgaria; Ass. Prof. Georgi Mishev - Medical Academy, Sofia, Bulgaria; Ass. Prof. Sara Sabatasso - University of Geneva, Switzerland; Ass. Prof. Raluca A. Ceausu - University of Timisoara, Romania.

Former students continuing their career in the clinic as medical doctors after MD theses in my lab (Last 10 years): Dr. Jehona Dzambazi, Dr. Ramona Triet, Dr. Raphael Rötthlisberger; Dr. Valerie Aurore-Schwartz; Dr. Milena Moretti; Dr. Thomas Koller; Dr. Miriana Savic; Dr. Mario Ropelato; Dr. Daniel Fries, Dr. Hannes Bangerter; Dr. Pascal Graa; Dr. Yosif El-Darawish; Dr. Silvan Boxler; Dr. Raphael Rötthlisberger; Dr. Cedric Zubler, Dr. Mathias Messerli.

Altogether I supervised more than 65 PhD, Master and MD theses. Last 5 years: 8 PhD, 16 MD theses and 6 Master theses. Long list of multiple awards and prices (could be provided).

Teaching activities:

Since years - broad spectrum of teaching activities (lectures, practical courses, workshops, tutorials, wet lab etc.) in Anatomy, Histology and Embryology in the following Study Programs: Medicine, Pharmacy, Veterinary Medicine, Biomedical Sciences, Biomedical Engineering, postgraduate Clinical Anatomy Courses for specialists. Responsible for the Anatomy curriculum and E-learning platforms in Anatomy at the University of Bern. Around 15h contact time per week plus 5h of administration and coordination.

Organization of scientific meetings:

Since 2007- Annually meetings of Swiss Clinical Anatomy (president since 2007)
 2017 - 10th Annual Swiss Zebrafish Meeting, Bern, Switzerland (<http://www.swisszebra.ch/>),
 2016 - 78th Annual Meeting of the Swiss Society of Anatomy, Histology, Embryology (SSAHE), Bern, Switzerland (http://www.ssahe.ch/meeting_2016.php),
 2015 - COST SYRA3, WG 1 Meeting, Bern, Switzerland (<https://www.syra3.eu/events>)
 2014 - COST SYRA3 4th MC meeting & 3rd WGs meeting, Bern, Switzerland, (<https://www.syra3.eu/events>)

Institutional responsibilities:

At the University of Bern, Switzerland:

2010-until now: Director of the Institute of Anatomy, Bern, with around 120 employees; Faculty Member, Graduate Student Advisor, Member of different Faculty committee (Structure, Internationalization, Recourses, Promotion, Succession etc.)

Membership in panels, boards and reviewing activities:

-2013-2017 Member Scientific Advisory Board supervision AngioMatTrain/EU7/ Marie Curie (<https://cordis.europa.eu/project/id/317304/reporting/de>)
 -2013-2017 Swiss representative and Vice Chair WG1 "Radiation Biology" SYRA3 COST Action TD1205 Innovative Methods in Radiotherapy and Radiosurgery using Synchrotron Radiation (<https://www.cost.eu/actions/TD1205/>)
 -Reviewer for numerous journals as Nature Comm, PNAS, EMBO, Radiation Research, Circulation, Circulation Res, Int J Radiat Oncol Biol Phys, Am J Pathology etc. (3-4 manuscripts per month) and founding agencies worldwide (SNSF, OncoSwiss, Bernese Cancer League, Wellcome Trust, ERC EU, Marie Curie, NovoNordisk, Natural Sciences and Engineering Research Council of Canada, NIH USA, Bulgarian Academy of Science, etc.). Evaluator infrastructural projects and academic positions in the field of Anatomy and bio-medical science (Switzerland, Germany, United Arab Emirates, USA, Bulgaria, Serbia, Ukraine, Romania, Czech Republic, Slovakia, Sweden etc.)

Active membership of scientific societies: since 1996: Swiss Society of Anatomy, Histology and Embryology (Past President), since 2003 Swiss Clinical Anatomy (acting president since 2007), since 2001: American association of anatomists (AAA), since 2001: European Anatomical Society (Anatomische Gesellschaft), since 2010: European Vascular Biology Organization (EVBO), since 2014: Radiation Research Society (RRS), European Society for Therapeutic Radiology and Oncology (ESTRO), 2017 Radiosurgery society (RSS).

Major collaborations:

Switzerland: Prof. J.A. Laissue (Uni Bern); Prof. D. Aebersold (Uni Bern); Prof. MC Vozenin (Uni Lausanne); Prof. T. Petrova (Uni Lausanne); Prof. C. Rueegg (Uni Fribourg); Prof. M. Fussenegger (Uni Basel); Prof. M Gassmann (Uni Zürich); Prof. A Banfi (Uni Basel); Prof. M Affolter (Uni Basel); Prof. S. Grabher (Uni Lausanne); Germany: Dr. S. Bartzsch (TUM), Prof. St. Combs (TUM), Dr. E. Schuelke (Uniklinik Rostock); Prof. F. le Noble (KIT); Prof. M. Ochs (Charite); Prof. A.R. Pries (Charite) Canada: Prof. C. Mothersill (McMaster University); Australia: Prof. J. Crosbie (RMIT); Prof. Olga Martin (Peter Mac), Prof. P. Rogers (Uni Melbourne), UK: Prof. U. Oelfke (ICR); France: Dr. Michael Krisch (ESRF), Prof. J. Balosso, Dr. R. Serduc, Prof. F. Esteve, Dr. A. Bouchet (UJF/CHU/INSERM/GIN); Finland: Prof. K. Alitalo (Uni Helsinki); Israel: Prof. E. Keshet; (Hadassah Med. School); Serbia: Prof. V. Volarevic and Prof. N. Filipovic (Uni Kragujevac); Romania: Prof. M. Raica and Prof. A Cimpean (Uni Timisoara) Italy: Prof. D. Ribatti (Uni Barri), Prof. A Bravin (Uni Milano Bicocca); USA: Prof. CR Harrell (Palm Harbor UFL), Prof. SW Jin (yale Univ. School); Bulgaria: Prof. I Dimova (Uni Sofia); Kenia: Prof. A Makanya (Uni Nairobi) and many others...

In the last 10 years, we concentrated on three main scientific directions which are linked together:

1) Microbeam Radiotherapy – a new hope for the future treatment of radioresistant tumors

Despite significant advances, the efficacy of radiation therapy for many radioresistant tumors remains suboptimal with current therapeutic doses. A new sophisticated technique, called Microbeam Radiation Therapy (MRT), allows for a higher dose prescription than conventional radiotherapy (CONV) without causing normal tissue complications. This is achieved with ultra-high dose rates (FLASH), orthovoltage photon energies, and non-uniform dose distribution. In preclinical studies, MRT significantly improved the therapeutic ratio compared with CONV in several cancer models with clinically poor prognosis, including radioresistant glioblastoma and melanoma.

In a mouse glioblastoma model, MRT, in combination with cisplatin, reduced tumor volume 6-fold compared with cisplatin alone and 60-fold compared to untreated mice. In a murine melanoma model, temporally fractionated MRT (133Gy x 3) ablated 50% of tumors and prevented organ metastases and local recurrences for 18 months after treatment. To our knowledge, this is the best treatment outcome ever achieved in any preclinical model. The radiation biology underlying the "MRT effect" appears to follow a completely new paradigm of radiation-induced tissue responses. In addition to killing tumor cells by extra-high peak radiation doses, several novel biological mechanisms contribute to treatment success: (i) In the range of 400-600 Gy, MRT selectively disrupts immature tumor vessels while sparing the mature vasculature of the surrounding normal tissue, implicating MRT as a completely novel, anti-angiogenic, tumor vascular-disruptive strategy; (ii) MRT peak doses in the range of 100-150 Gy temporally increase tumor vascular permeability, creating a transient "transpermeability window" that has been identified as an efficient drug delivery system with high therapeutic potential; (iii) tumor vessels disrupted by MRT serve as a gateway for circulating immune cells to invade tumor tissue, resulting in enhanced anti-tumor immune responses; (iv) gene expression analysis of MRT-irradiated tumors identified a specific gene signature for an 'MRT-induced immune effect', involving myeloid cell recruitment and interferon responses. These unique features support MRT as a novel therapeutic approach for the treatment of inoperable, radioresistant lesions.

2) Intussusceptive angiogenesis as an alternative type of normal vascular formation, regeneration, and carcinogenesis :

Intussusceptive angiogenesis (IA, described for the first time by our group) takes place not only during physiological processes but is also a critical component of different diseases including tumor growth, colitis, and neurotoxic disease, among others. IA is essential for formation and restoration of an organ-specific angioarchitecture. IA plays an important role as an "escape" mechanism of the tumor vasculature after irradiation or anti-VEGF-therapy. We revealed the following key findings: during early zebrafish and chick development, as well as fin regeneration, the formation of the primitive vascular plexus was initiated by sprouting angiogenesis (SA) but further vascular growth, pruning and remodeling occurred by IA. We demonstrated that SA and IA have different underlying regulatory mechanisms. In contrast to SA, which is activated mainly by growth factor gradients such as VEGF, IA was driven mainly by blood flow and vascular splitting and pruning were induced by a particular shear stress profile. In this way, we proposed a novel hypothesis combining SA with IA as a result of alterations in a predetermined genetic program for vascular patterning induced by hemodynamic forces.

3) Vascular imaging, with a focus on using novel, non-destructive microangio-CT for the visualization and quantification of whole-organ vasculature:

In most animal models, the non-destructive investigation of the whole-vasculature down to the capillary level was not feasible. We developed a conceptually new non-destructive ex-vivo microangio-CT (μ aCT) to visualize and quantify the entire vasculature of an organ including the capillaries (in a range of 4-6 μ m in diameter). In addition, a new polymerizing contrast agent (μ Angiofil) was developed, with autofluorescent properties that allow for correlative analysis. Moreover, subsequent morphological analyses by histology, immunohistochemistry, classical transmission-electron microscopy, and/or 3D-serial block face-scanning electron microscopy can be performed after microangio-CT scanning. The μ aCT-based protocols we introduced for vascular quantification are superior to and faster than the time-consuming classical morphometry. Validation based on lectin-stained histological sections revealed excellent perfusion efficiency. By applying this approach, we analyzed normal vasculature and pro- and anti-angiogenic treatment strategies in murine brain, kidney, muscle, eye, heart and bones. We introduced a correlative and quantitative imaging approach that is highly reproducible and allows, for the first time, a detailed 3D characterization of the whole-vasculature down to single capillary vessels. Alone, or as a correlative approach in combination with histology and electron microscopy, this methodology opens new horizons for a broad-range of investigations in the field of vascular biology.

Publication metrics (Web of Science)

Total Publ.: 256 ; h-index: 61	Sum of Times Cited: 13851	Average citations per item: 54.01
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Publication List: <https://pubmed.ncbi.nlm.nih.gov/?term=djonov&sort=pubdate>

In the last 10 years Original publications: 108, review articles: 36. In addition, 8 Book chapters

* = Djonov senior author

My group described for the first time that MRT is sparing healthy lungs from pulmonary fibrosis and that various other types of normal tissues are also highly tolerant to MRT:

- *Trappetti V,... **Djonov V:** Targeted Accumulation of Macrophages Induced by Microbeam Irradiation in a Tissue-Dependent Manner. *Biomedicines*. 2022 Mar 22;10(4):735.
- *Trappetti V,... **Djonov V:** Synchrotron Microbeam Radiation Therapy for the Treatment of Lung Carcinoma: A Preclinical Study. *Int J Radiat Oncol Biol Phys*. 2021;6:50360-3016(21)02630-4.
- *Wright MD, ... **Djonov V:** FLASH microbeam radiotherapy provides superior normal tissue sparing in rat lung compared to FLASH radiotherapy. *Cures* 2021;13(11):e19317
- *Potez M, ... **Djonov V:** Effects of Synchrotron X-Ray Micro-beam Irradiation on Normal Mouse Ear Pinnae. *Int J Radiat Oncol Biol Phys*. 2018 Jul 1;101(3):680-689.

We reported for the first time that MRT induces selective vascular disruption in immature/tumor vessels while preserving normal, mature vasculature and that low dose MRT increases vessel permeability and serves as a very effective drug delivery strategy for combined cancer treatment:

- *Brönnimann D,... **Djonov V:** Synchrotron microbeam irradiation induces neutrophil infiltration, thrombocyte attachment and selective vascular damage *in vivo*. *Sci Rep*. 2016 Sep 19;6:33601.
- *Sabatasso S, ... **Djonov V:** Microbeam radiation-induced tissue damage depends on the stage of vascular maturation. *Int J Radiat Oncol Biol Phys*. 2011 Aug 1;80(5):1522-32.
- *Sabatasso S, ... **Djonov V:** Transient and Efficient Vascular Permeability Window for Adjuvant Drug Delivery Triggered by Microbeam Radiation. *Cancers (Basel)*. 2021 Apr 27;13(9):2103.
- *Bouchet A,...**Djonov V:** Effects of microbeam radiation therapy on normal and tumoral blood vessels. *Phys Med*. 2015 Sep;31(6):634-41. (Review)

We demonstrated that MRT achieved excellent tumor control in a radioresistant melanoma model and temporally fractionated MRT successfully resulted in complete tumor eradication:

- *Trappetti V,... **Djonov V:** Microbeam Radiation Therapy controls local growth of radioresistant melanoma and treats out-of-field locoregional metastasis *Int J Radiat Oncol Biol Phys – in press*
- *Potez M,... **Djonov V:** Synchrotron Microbeam Radiation Therapy as a New Approach for the Treatment of Radioresistant Melanoma: Potential Underlying Mechanisms. *Int J Radiat Oncol Biol Phys*. 2019 Dec 1;105(5):1126-1136.
- *Fernandez-Palomo C,... **Djonov V:** Complete Remission of Mouse Melanoma after Temporally Fractionated Microbeam Radiotherapy. *Cancers (Basel)*. 2020 Sep 17;12(9):2656.
- *Trappetti V,... **Djonov V:** Microbeam Radiotherapy-A Novel Therapeutic Approach to Overcome Radioresistance and Enhance Anti-Tumour Response in Melanoma. *Int J Mol Sci*. 2021 Jul 20;22(14):7755. (Review)
- *Fernandez-Palomo C, ... **Djonov V:** Animal Models in Microbeam Radiation Therapy: A Scoping Review. *Cancers (Basel)*. 2020 Feb 25;12(3):527. (Review)
- *Potez M,... **Djonov V:** Characterization of a B16-F10 melanoma model locally implanted into the ear pinnae of C57BL/6 mice. *PLoS One*. 2018 Nov 5;13(11):e0206693.

We have continued to investigate intussusceptive angiogenesis (described for the first time in our group) as an alternative process for blood vessel formation during tissue regeneration and tumorigenesis:

- *Senk A, **Djonov V:** Collagen fibers provide guidance cues for capillary regrowth during regenerative angiogenesis in zebrafish. *Sci Rep*. 2021 Sep 30;11(1):19520.
- *Dimova I,... **Djonov V:** SDF-1/CXCR4 signalling is involved in blood vessel growth and remodelling by intussusception. *J Cell Mol Med*. 2019 Jun;23(6):3916-3926.
- *Karthik S,... **Djonov V:** Synergistic interaction of sprouting and intussusceptive angiogenesis during zebrafish caudal vein plexus development. *Sci Rep*. 2018 Jun 29;8(1):9840
- Grunewald M, ...**Djonov V**, ... Keshet E: Counteracting age-related VEGF signaling insufficiency promotes healthy aging and extends life span. *Science*. 2021 Jul;373(6554):eabc8479.

We introduced for the first-time worldwide, the novel, non-destructive microangio-CT method for the visualization and quantification of whole-organ vasculature down to the capillary level:

- *Hlushchuk R, ...**Djonov V.** Innovative high-resolution microCT imaging of animal brain vasculature. *Brain Struct Funct*. 2020 Dec;225(9):2885-2895.
- *Hlushchuk R, ..., **Djonov V:** Cutting-edge microangio-CT: new dimensions in vascular imaging and kidney morphometry. *Am J Physiol Renal Physiol*. 2018 Mar 1;314(3):F493-F499.
- Räsänen M, **Djonov V**, ... Alitalo K: VEGF-B Promotes Endocardium-Derived Coronary Vessel Development and Cardiac Regeneration. *Circulation*. 2021 Jan 5;143(1):65-77
- *Schaad L,... **Djonov V.** Correlative Imaging of the Murine Hind Limb Vasculature and Muscle Tissue by MicroCT and Light Microscopy. *Sci Rep*. 2017 Feb 7;7:41842.

Patents US20160128983A1: Cytotoxic substance for use in combination with radiotherapy in cancer treatment
Patent F05388: Contrast Agent for Microangiography