投稿被判死刑后怎么办？ 上诉成功（一）

数年寒窗做研究，好不容易完成了一篇文章，慎重选好了杂志投稿，然后满怀期望地等待消息，不料被一封礼貌但冷酷的编辑来信把希望浇灭。这个过程做科研的人大概都曾经历过，我们也不例外。

被杂志判死刑理由不外以下几点，一是文章内容本身有问题；二是杂志选的不对路；三是编辑或审稿人水平低和误判。前两种原因没什么可说的，被拒应该。我这里重点说第三种。我们研究组的人在被误判瞎判情况下基本不会认命，总有一个会出面据理力争，结果是好几篇被那些主编们匆匆判了死刑的文章经过据理力争后居然败步复活了，当然这样的例子并不多。更多的时候我们先是怒火万丈说编辑审稿人有眼不识泰山，冷静下来后读读 reviewing 中有什么有价值的意见，找到中肯的意见后就老老实实修改，完成后改投更高一级或更适合杂志，这个成功比例比较高。这里我想将有些经验写下来，供国内同行参考。

2003 年开始我们做了一系列兔子眼睛的实验，用一个很敏感细小光纤探针测量兔眼中氧分子浓度分布以及在不同供氧状态下眼内氧浓度动态变化。我们想通过这个实验间接了解人眼中氧分子浓度的分布情况，以便探讨一些与眼科疾病发病的有关机理。

这说起来容易做起来还蛮复杂的。为了真实的模拟正常生理状况，我们要求麻醉师给兔子全麻后气管插管，用呼吸器控制肺部的氧分压和监测血氧饱和度，一切要与兔子正常安静非麻醉状态的情况相似，然后调节氧浓度到机体最大和最低可承受范围。可以想象给全麻下的兔子给高氧根本不是问题，但降低氧浓度是个难题。麻醉师开始拒绝做低氧实验，说翻开所有医学书，没听说过全麻时不但不额外供氧，竟然还降低氧的浓度，不干！在反复解释其意义后麻醉师终于答应配合。在实验中除了手术步骤仔细轻巧外，在调节供氧和麻醉过程也异常小心，一次实验需要 4~5 小时左右。在实验期间我们失败了好多次，但几十次手术实验下来我们得到了许多意想不到的好结果，其创新及意义对我们后来在人体上的实验奠定了坚实的基础。

我们把这个研究结果写成论文投稿到眼科专业比较有影响的杂志 IOVS。通常杂志主编或专业编辑选择二至三名同行来审稿，每人都有一票否决权。万一意见两极或争议较大，编辑有最后生杀决定权。编辑的结论有时象最高法院判决，不能再上诉了。

交稿后一个月左右就有了回复，回复很干脆：IOVS 拒绝发表。理由呢？仔细阅读了三位审稿者的内容，除了有些建议，提问和修改的意见外，大部分都是肯定的，而且三位审稿人均提议少许修改后可以发表。问题出在编辑上！编辑不理睬三位审稿人的意见，自己写了他否定的理由。

当教授拿着编辑的判决信来找我时脸上阴云密布，他说我们是否考虑转投低一级的杂志。我认真读完了编辑的判决书，突然放心地笑起来了。我告诉教授；放松点，这回我们肯定要推翻“最高法院判决”，原因也很干脆：主编犯了个非常低级的错误。

问题出在一个图上。我们把眼内各部位氧分压分布标在一个兔眼睛平面示意图上，数据一目了然（见图 1）。而主编拒绝采用本文的原因是当他看到这个图，他想象中为了把光纤探针放到如图所示眼内各部位，实验者“必须”把整个兔眼睛拽出眼眶，这样会造成供应眼球血

液的眼动静脉严重扭曲牵拉，因此他认为仅由此一图，这个研究的全部氧浓度的测定根本不可靠，不必再往下看了，浪费时间，枪毙了事。

这理由真荒唐，我忍不住脱口道这家伙压根不知道怎么做眼科手术，一定是一个搞基础研究的 PhD。在美国 MD(医生)和 PhD(研究博士)互相瞧不起，临床和基础研究脱节的厉害。这个堂堂 IOVS 编辑居然凭想象手术样子枪毙一篇文章，看样子得教教他眼科手术的基本 ABC。看我轻松的样子，教授和同事们一头雾水，我突然想起教授也是一个 PhD 出身，他大概被主编的想象朦住了，以为我们做错了，不然他这样的科学家不会这么沮丧的。我安慰他说补做一次实验就可明白了，此时我在中国接受的 MD 背景帮上了大忙。

下次实验时除了平时两个助手，我多带了一个秘书丽莎，她在手术台外只负责一件事，给手术过程拍照，大约拍了 50~60 张。回来后我用幻灯先给科里的 PhD 们和技术员讲解眼科手术的基本要点和注意事项，大家听后都明白了在测量眼内氧浓度时，我们既没有把兔眼睛拽出眼眶，也没有给眼球额外加压。为了避免任何干扰眼血液供应，我们连常规的开睑器都不用，只用了一个角膜接触镜，任何眼肌的牵拉都严禁，实验结果没有任何问题。本来大家想去幽默一下这个自以为是的主编，可情绪化语言是专业中的一个禁忌，我们只能客观地描述了手术中为了避免不必要人为误差改变，我们所有操作是在眼球原始位严格进行的，那里需要把眼球拽出眼眶？（图 2）我们选了两张手术测量中照片附在给编辑的回信中，同时我们还对其他审稿人提的良好建议和问题一一作了回答和修改。一周后主编回信，论文被接受并尽快会发表，对他自己的武断表示了诚挚的歉意。

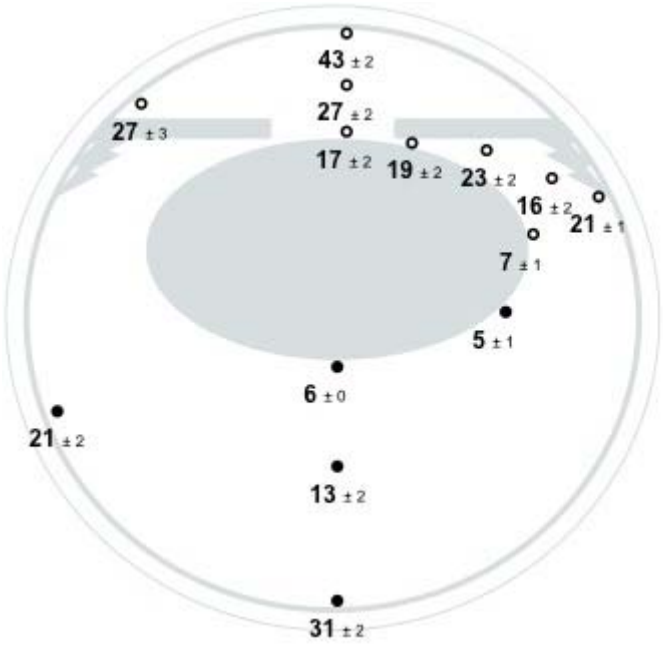


图 1：pO^2 在正常兔眼内分布图。此图让编辑误解了我们是将眼球拉出眼外做的实验。

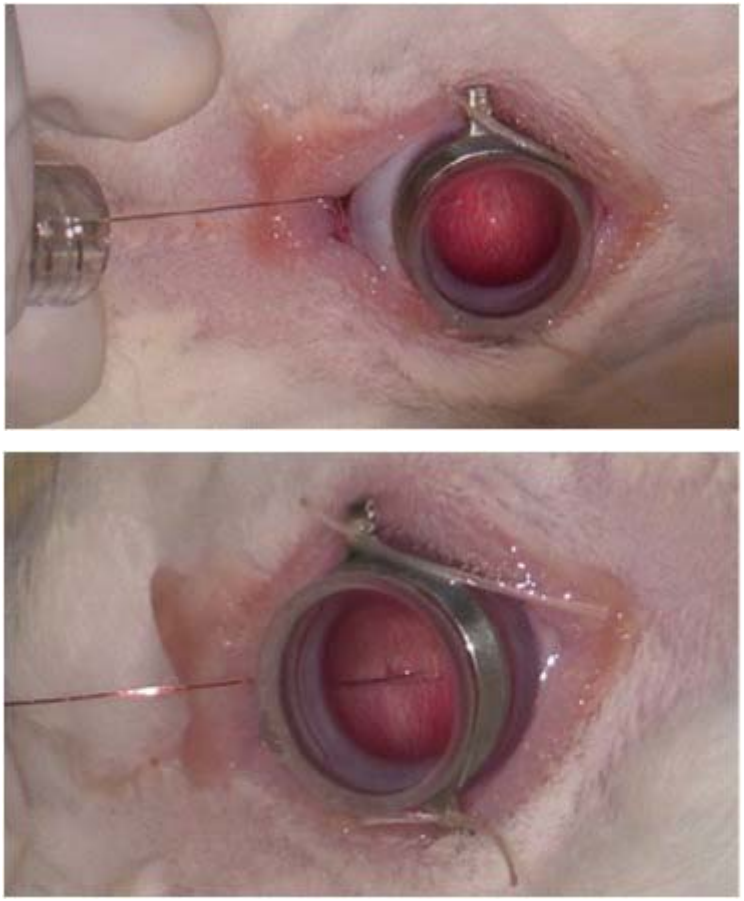


图 2：光纤探针插人眼内测量不同状态下的氧浓度，眼球完全不需要“拽出来”。

感想之一：IOVS 编辑尽管犯了先入为主的主观错误，他也非常正派。一旦认识到自己错了，立刻就改，由衷佩服！

感想之二：自己的实验一定要有坚实的土壤，要自信不要轻易被别人的否定，那怕是大人物的否定所吓倒，当然如果实验是假的或瞎胡弄的例外。

投稿被判死刑后怎么办？ 上诉成功（二）附申述信要点

上篇讲到我们投稿遇上认真的审稿人但编辑却一时糊涂，我们用事实让编辑改判使得文章顺利发表。这回要说的是更倒霉更不幸的是碰上了一个不负责任的编辑，他 / 她压根没告诉我们审稿人的意见是什么，一人大包大揽，以 Editorial Board comments 名义把我们的文章草草毙了。大家本不想浪费时间改投其它杂志，可偏偏碰上了我们一个爱较真的 MD，她受不了 review 中错误百出的评议，一通毫不含糊反驳 email 直接送到主编手里，她的 email 火药味很浓但每条理由充分，让主编不得不认真读了原文再看他们杂志的 review，主编为他们编辑和审稿人的水平汗颜，于是主编越过原审稿人和编辑亲自审阅原稿，修改稿以及终稿，在我写这个故事的今天，该文已发表在 Am J Ophthalmol (Internet Advance) 上了。全文请查：http://www.ajo.com/inpress

现在想把重点放在申述信上。本人欣赏这封信，自惭英文有限难写出这样有理有力的申述信，介绍给中国有兴趣同行们是希望它山之石，可以攻玉。

先介绍一点有关研究背景：白内障是眼科发病率最高的眼疾，在发展中国家是致盲首因，在发达国家虽可用现代手术方法治愈，但费用昂贵占所有眼病中首位。到目前为止我们对其发病机理知之甚少，预防更是一句空话。我们小组经过近十年的系列基础和临床实验研究，提出了眼内分子氧的内环境改变与常见的核性白内障发病有密切关系。然而证实这个理论有难以想象困难，其原因有三：

1)　此类研究只能在活体(in vivo)上进行，体外实验只能作为辅助研究；
2）动物眼的解剖生理生化无法与人眼相拟，例如玻璃体切除术后核性白内障只发生在人类，迄今为止尚无法成功建立类似动物模型；
3） 人的活体研究有非常严格的限制，只能利用某些特定疾病治疗时并在病人同意下做些观察研究。

幸运的是我们有一个包含 MD 和 PhD 在内的有共同研究志向团结一心的 team，有良好的基础和临床相结合的研究经验，有广泛支持我们并志愿参加研究的病人群体（美国的病人大多乐意为科研作贡献）。具体到本次论文课题，我们认为人眼的水晶体是一个特殊器官，无血管无神经，它生存在一个低氧环境（<1%) 所以代谢及生长缓慢，能长期保持透明和弹性。一旦低氧环境被破坏如玻璃体视网膜手术或玻璃体液化（通常表现为飞蚊症），从视网膜血管网来的高浓度分子氧会长驱直入水晶体，其 oxidative stress 导致了水晶体核逐渐变硬变混形成白内障。以上这都是纸上谈兵的理论，要证实这个理论是否正确却不简单：即设法证实眼内低氧环境能保护水晶体；而高氧环境会导致核性白内障。我们文章的题目是：Ischemic Diabetic Retinopathy May Protect Against Nuclear Sclerotic Cataract。此研究利用缺血性糖尿病视网膜病变作为典型低氧模型，用玻璃体切除术后眼内形成较高氧浓度情况为对照，定量追踪观察水晶体变化一年左右，结果证实了低氧环境确实可以保护水晶体。

好了，言归正传，该说到伸述信了。英文部分是来自原文节选，中文是本人加入的少许解释。

.....I am writing to you about my concerns regarding the quality of reviewers for a paper rejected by the AJO, but in this situation I am the author. I do not wish to appear as a "disgruntled author" as my manuscripts have been rejected many times before without formal complaint. On this occasion I merely wish to express my concern that the reviewers did not carefully read nor have the necessary background to judge the manuscript. Allow me to explain. (开场白，此信主要目的是针对编辑的审稿水平)。

1. "*A Case-Control study design seems to be more appropriate to prove their hypothesis*". （蓝色斜体字是编辑的意见，下同）

Prior to submission, all of the authors debated this subject at length and unanimously agreed that a prospective cohort study better described our 2 years of prospectively accumulating quantitative data. We came to that conclusion after studying the following definitions: Cohort study and Case-control study..... (名词解释见后). In light of these definitions, I would like to suggest to the reviewer that a case-control study would not be any better than the prospective cohort study in proving the hypothesis presented in the manuscript.（我们确实 email 来往不下几十次讨论学习直到大家都弄明白为止，此编辑大概没好好思索过在这个基本概念上有些不清楚。）

2."*Diabetic patients usually have higher incidence of cortical lens opacity, and cortical opacity also influences visual function such as nuclear cataract. If they had provided a more detailed description of cataract progression according to cortical opacity, posterior capsular opacity and nuclear opacity, this may have more clinical significance*."

The Scheimpflug camera that we used to objectively grade the progression of nuclear opacities also provides retroillumination images that can be used to quantify the extent of cortical and posterior subcapsular cataracts. Any changes in these opacities would have been evident. Only nuclear opacities progress after vitrectomy. A knowledgeable reviewer would have known this basic information. （白内障有三种类型，每种的发病机理各不同，糖尿病常引起皮质性和后囊下白内障，而玻璃体切除术术后主要引起核性白内障。编辑在这个问题上混淆不清，缺乏应有的专业知识。）

3. "*The authors had previously reported in the 2006 AJO that diabetic eyes have lower intraocular oxygen tension compared with non-diabetic eyes, thus, have lesser nuclear sclerosis cataract. Given such, it is questionable that this article really presents any additional findings or stronger evidences compared to their previous report*."

We are pleased that the reviewer is aware of our 2006 AJO paper showing that diabetic eyes have a lower intraocular oxygen tension compared with non-diabetic eyes. However, in our previous study, we proposed that diabetics would have slower progression of nuclear cataract after vitrectomy. The present study was the test of this hypothesis. It would be scientifically inappropriate to assume that having lower oxygen would protect against nuclear cataract without testing this theory. The present manuscript, for the first time, prospectively gathers quantitative data on nuclear cataract and demonstrates that ischemic diabetic eyes have less nuclear sclerotic cataract. （编辑认为我们在以前文章中提出了设想就足已，对于这篇证实原假设的研究觉得没有必要了？这个错犯的太低级了。）

4. "*This study lacks sufficient evidence that the presence of ischemia than diabetes itself was more associated with delayed nuclear opacity because they did not directly compared ischemic diabetic retinopathy eyes with background diabetic retinopathy eyes*."

This reviewer simply did not read the manuscript carefully. The Results section states, "Table 3 shows the average nuclear light scattering units as measured by Scheimpflug photography before and after vitrectomy in the non-diabetic eyes and the non-ischemic diabetic eyes undergoing surgery for non-diabetes related conditions such as macular hole and macular pucker. There was no statistically significant difference between these two groups. Therefore, for the purpose of the analysis, these non-diabetic and non-ischemic diabetic eyes were collectively grouped as "non-ischemic" eyes for comparison to eyes with ischemic diabetic retinopathy." The non-ischemic diabetic eyes either had no retinopathy or background diabetic retinopathy, but they behaved post-vitrectomy just like non-diabetic eyes. Therefore, this paper showed that it was not the presence of diabetes that protected against post-vitrectomy nuclear cataract but rather the presence of ischemic diabetic retinopathy. （任何研究人的疾病都是复杂的，不能如动物实验

设定相同条件，我们必须根据病人患的疾病以及程度细细区别。编辑提的问题我们有详细回答，可惜他／她没有耐心读完就下了结论，自然被拍砖了。）

5. "*Age is the strongest factor which influences the development of postoperative nuclear sclerosis formation even in diabetic patients. Even though authors adjusted age factor using statistical analysis (multiple regression analysis), their very limited number of cases (at 12 months, n=5 vs. n=10) brings to question the reliability of their statistical results*."

We agree that age is an important factor influencing the development of post-vitrectomy nuclear sclerotic cataract. That is why we performed a multiple regression analysis. We acknowledge that we had a small number of cases. That is why we used prospectively obtained Scheimpflug photographs. Scheimpflug photography allows the researcher to objectively quantify NS cataract so that meaningful comparisons can be made with only small numbers of patients. We have fulfilled our scientific obligations. It is not appropriate to question the reliability of the result based only on the number of subjects. One uses statistics to demonstrate that, given the number of subjects enrolled, the differences in the groups are or are not significantly different. In this study, the differences between ischemic and non-ischemic eyes at 12 months post vitrectomy were large and highly significant (p=0.001).

Finally, it should also be recognized that an important reason for the smaller number of cases in which opacity could be quantified at 12 months was that half of the non-ischemic cases had already had cataract surgery (as compared to only one of the ischemic subjects), thereby precluding analysis by Scheimpflug photography. This result further demonstrates the protective effect of ischemia.（补充，编辑说我们例数少了没错，但为什么少了是部分病人因为白内障发展太快不得不做了手术，这从另方面证实了结果的一致性。在修改本中，我们增加了后来半年的例数重新分析了结果。）

6. "*Gas tamponade is one of the known cataract aggravating factors. There were 17 cases of macular hole surgeries and 4 cases of retinal detachment surgeries included in the non-ischemia group. Was gas tamponade used in these cases?*"

Again, the reviewer did not carefully read the manuscript. The last sentence of the Results sections states, "Gender, race, surgical eye, gauge of surgery (i.e. 20, 23, 25 gauge vitrectomy), or use of intraocular gas tamponade were not significantly associated with nuclear opacity after vitrectomy (not shown)." In addition, we are about to submit for publication a manuscript that proves (again via prospectively obtained Scheimpflug data) that gas tamponade does not aggravate post-vitrectomy NS cataract. Thus, the reviewer has an incorrect,
unproven bias on this topic. (编辑显然是一个懂眼科手术内行，但是不仔细读完全文就下结论不挨砖才怪。）

7. "*There are issues concerning the novelty of the observations, and ability of the small sample size to answer the scientific question of whether it is ischemic retinopathy or diabetes itself that protects against nuclear cataract.*"

A careful reading of our manuscript would indicate that, in fact, this is new information collected prospectively using Scheimpflug technology to compensate for the small sample size. Our statistical results are significant across the board (and not marginally so). Finally, it is quite clear from the data presented that it is the presence of ischemic retinopathy alone and not merely the presence of diabetes that protects against post-vitrectomy NS cataract. This is a novel finding. It is an important finding. It corroborates the growing hypothesis that the oxygen source for nuclear sclerotic cataract in all persons is the retina and perhaps the other vascularized tissues of the eye. （做临床研究，样本数永远是一个 issue，这点我同意编辑的意见，但实际操作要看具体情况和方法。）

8. "*Lower priority score*."

The reviewers have failed to recognize one of the most important insights arising from this manuscript. By studying and understanding the lack of progression of post-vitrectomy nuclear sclerotic cataract in eyes with ischemic diabetic retinopathy, a novel strategy for preventing nuclear sclerotic cataract in eye becomes apparent: simply reduce the amount of molecular oxygen reaching the crystalline lens. Thus, we now have, for the first time, a rational approach for preventing the leading cause of blindness in the world. This merits a high priority score. (尽管我对本课题的研究结果和意义非常有信心，要我这么毫不客气高度评论自己的文章，以中国文化传统，我还真做不到。可我们这位 MD 自信满满地做到了，这是我深为感慨和佩服的地方。）

收到此信后 AJO 主编很快回复，下面是主编的第一次回信内容：“Yes, the reviewers did seen somewhat misguided. I have granted you a rebuttal for this manuscript and then you can do some revision and resubmission. You should have received that notice. Please include the comments below in the cover letter.”

后来呢？读者可以自己推理了。